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Siloxane derivatives of 2-mercaptobenzothiazole

Larisa V. Zhilitskaya,* Nina O. Yarosh, Lyudmila G. Shagun, Ivan A. Dorofeev and Lyudmila I. Larina

A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 664033 Irkutsk, Russian Federation. Fax: +7 3952 419 346; e-mail: lara_zhilitskaya@irioch.irk.ru

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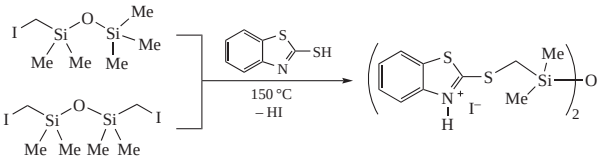
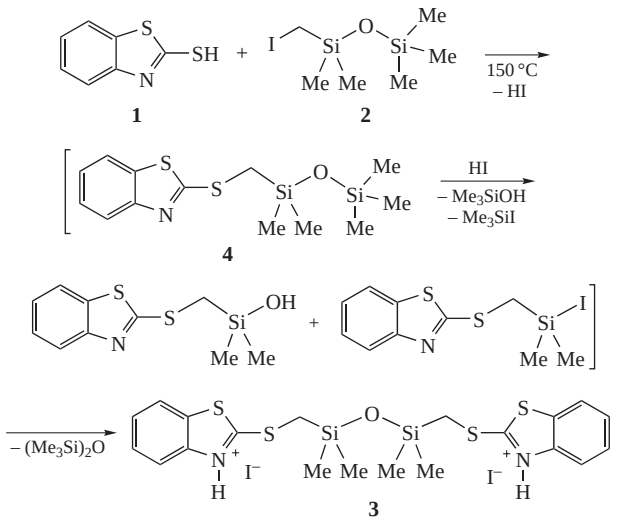
First organosilicon captax derivatives were obtained from 2-mercaptobenzothiazole and 1-(iodomethyl)-1,1,3,3,3-pentamethyl- or 1,3-bis(iodomethyl)-1,1,3,3-tetramethyldisiloxanes in the absence or in the presence of bases.



2-Mercaptobenzothiazole (captax) **1** and its derivatives are biologically active compounds possessing antibacterial, fungicide, anticonvulsive, anti-inflammatory, antitumor, antioxidant and antiallergic properties.[1] In industry, captax is employed as inhibitor of metal corrosion, vulcanization accelerator,[2] and promising luminescent material.[3] Therefore, the investigations in this field may result in discovery of novel unexpected properties and application areas of such compounds. We assumed that introduction of the tetramethylsiloxane groups into a molecule of industrial 2-mercaptobenzothiazole should impart elasticity, strength, chemical inertness and biocompatibility to the products.[4]

The classical method for derivatization of 2-mercaptobenzothiazole involves alkylation with haloalkanes in the presence of bases[1,5] (KOH, K_2CO_3, NaOMe, C_5H_5N) in water, ethanol, acetone, sometimes on using ultrasound[6] or microwave irradiation.[7] The reaction with acyl chlorides affords a mixture of N- and S-acylated products.[8] Alkylation of S-alkylated 2-mercaptobenzothiazoles with iodoalkane bearing the same alkyl group proceeds across the nitrogen atom to deliver S,N-dialkylated salt.[9] The data on alkylation of 2-mercaptobenzothiazole with iodomethyl derivatives of siloxane are lacking in the literature. Meanwhile, the employment of these compounds in the reaction with captax can provide a series of novel functionalized benzothiazoles.



Scheme 1

In this work, we have implemented the reaction of 2-mercaptobenzothiazole **1** with mono- and bifunctional electrophilic reagents, 1-(iodomethyl)-1,1,3,3,3-pentamethyl- and 1,3-bis(iodomethyl)-1,1,3,3-tetramethyldisiloxanes, in various media.

We expected that solvent- and base-free alkylation of **1** with 1-(iodomethyl)-1,1,3,3,3-pentamethyldisiloxane **2** on heating would furnish S,N-dialkylation products, which under these conditions could form cyclic polyiodides in one preparative step[10,11] owing to the presence of labile iodomethyl moiety and flexible siloxane bond in the molecule of the alkylating agent. Contrary to these expectations, this reaction at 150 °C proceeds selectively (^{1}H, ^{13}C, ^{15}N NMR monitoring) at the mercapto group to give bis-salt **3** in 48% yield (Scheme 1).†

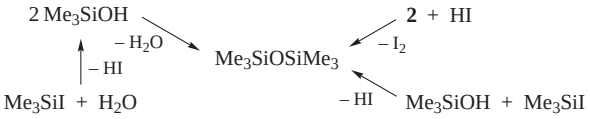
The key step of the reaction is the cleavage of siloxane bond[12] in adduct **4** under the action of hydrogen iodide, which is released

† IR spectra were recorded on a Vertex 70 Bruker instrument for KBr pellets (compounds **3**, **6**) and for thin film samples (**4**). ^{1}H, ^{13}C, ^{29}Si, and ^{15}N NMR spectra were measured on Bruker DPX-400 and Bruker AV-400 at 400.13, 100.61, 161.98, and 40.56 MHz, respectively. Chemical shifts are given relative to TMS (^{1}H, ^{13}C, ^{29}Si) and $MeNO_2$ (^{15}N). 2D ^{1}H-^{15}N NMR spectra were recorded using HMBC-gp ^{1}H–^{15}N correlation technique. The elemental composition was determined on a Thermo Scientific Flash 2000 automatic CHNS-analyzer. The iodine content was determined by mercurimetric titration, silicon was determined by dry combustion method. Melting points were determined on a Micro-Hot-Stage PolyTherm A apparatus. The reaction course and the compounds purity were monitored by TLC (Silufol UV-254 plates, acetone as an eluent).

Reaction of compound **1** *with* **2** *or* **5** *(general procedure)*. A mixture of 2-mercaptobenzothiazole **1** (0.2 g, 1.2 mmol) and iodomethyldisiloxane **2** (0.35 g, 1.2 mmol) or **5** (0.25 g, 0.6 mmol) was stirred at 150 °C for 3 h until the consumption of iodide (^{1}H, ^{13}C NMR monitoring), and then cooled to room temperature. Then acetone (15 ml) was added, the precipitate of salt **3** was filtered off, washed with acetone and diethyl ether, and dried in vacuum.

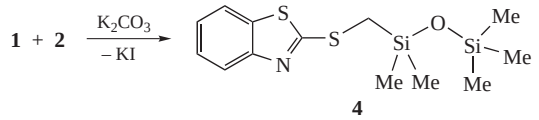
2-{[3-(1,3-Benzothiazol-2-ylsulfanyl)methyl]-1,1,3,3-tetramethyldisiloxanylmethyl}sulfanyl-1,3-benzothiazole dihydroiodide **3**. Yield 0.43 g (48%, from **2**), 0.36 g (81%, from **5**), white powder, mp 146–148 °C. IR (KBr, ν/cm^{-1}): 1076 (Si–O–Si). ^{1}H NMR (DMSO-d_6) δ: 0.18 (s, 12H, Me), 2.66 (s, 4H, CH_2S), 7.30 (dd, H^4, $^3J_{HH}$ 8.2, 8.6 Hz), 7.41 (dd, H^8, $^3J_{HH}$ 8.4, 8.6 Hz), 7.76 (d, H^9, $^3J_{HH}$ 8.4 Hz), 7.89 (d, H^4, $^3J_{HH}$ 8.2 Hz), 9.70 (br. s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ: 0.08 (Me), 19.17 (CH_2), 121.56 (C^4), 124.05 (C^{5,6}), 126.19 (C^7), 134.58 (C^8), 152.85 (C^9), 169.38 (SC). ^{15}N NMR (DMSO-d_6) δ: –105.9. ^{29}Si NMR (DMSO-d_6) δ: 5.2. Found (%): C, 32.06; H, 3.30; I, 33.84; N, 3.56; S, 16.95; Si, 8.34. Calc. for $C_{20}H_{26}I_2N_2OS_4Si_2$ (%): C, 32.08; H, 3.50; I, 33.90; N, 3.74; S, 17.13; Si, 7.50.

in situ. This likely leads to intermediates (see Scheme 1) giving finally bis-salt **3** and hexamethyldisiloxane. The latter can also be formed *via* condensation of trimethylsilanol or reduction of the iodomethyl function of siloxane **2** with hydrogen iodide (Scheme 2). Formation of intermediate **4** (see Scheme 1) and hexamethyldisiloxane is confirmed by the signals of silicon atoms at 9.4, 3.3 and 7.0 ppm [typical of $OSiMe_3$, SCH_2SiMe_2 and $(Me_3Si)_2O$] in the ^{29}Si NMR spectra of the reaction mixture.



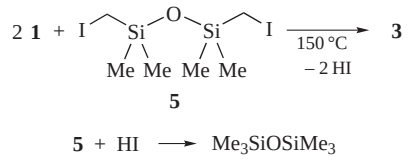
Scheme 2

The reaction of 2-mercaptobenzothiazole **1** with monoiodide **2** under classical conditions, which exclude formation of hydrogen iodide and cleavage of the Si–O bond, affords hitherto unknown siloxane sulfide **4** in 87% yield (Scheme 3).‡



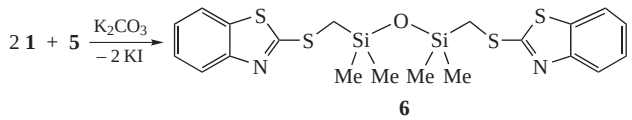
Scheme 3

Earlier[10] we have shown that compound **2** under the action of hydrogen iodide easily disproportionates to bis(iodomethyl)-1,1,3,3-tetramethyldisiloxane **5** and $(Me_3Si)_2O$. Therefore, it is not improbable that diiodide **5** can act as alkylating agent in the base-free reaction of thiol **1** similarly to monoiodide **2**. We assumed that bis-salt **3** could be synthesized by alkylation of 2-mercaptobenzothiazole with bifunctional electrophile **5** in a higher yield due to decrease of the losses related to cleavage of the Si–O bond (Scheme 4).† In fact, the reaction proceeds at the mercapto group involving both iodomethyl fragments of siloxane **5** to produce compound **3** in 81% yield (^1H, ^{13}C, ^{15}N NMR data). The ^{29}Si NMR spectrum of the reaction mixture contains, apart from a signal of the silicon atom at 5.2 ppm (SCH_2SiMe_2), a small signal in the region of 7.0 ppm assigned to $(Me_3Si)_2O$, which is apparently formed upon partial reduction of two iodomethyl groups of the initial disiloxane **5**.



Scheme 4

When this reaction is carried out in acetone solution in the presence of K_2CO_3, non-salt adduct **6** is formed in 90% yield (Scheme 5).‡



Scheme 5

It is known that the reaction of S-alkylated 2-mercaptobenzothiazoles with iodoalkanes proceeds at the nitrogen atom for 50 h to deliver S,N-dialkylated salt.[9] We also attempted to synthesize analogous dialkylated salt from reactants **2** and **4** (solvent-free, 150 °C, 6 h). According to the ^1H NMR data, the ratio of this product to the starting compound **4** was 1:1. In the ^1H NMR spectrum, a proton signal appeared at 4.13 ppm, while in 2D ^1H–^{15}N HMBC NMR spectrum, a cross-peak (–205.5 ppm) between nitrogen atom and CH_2 group protons was observed (for **3** this value corresponds to –105.9 ppm). Optimization of the conditions should increase preparative yield of the target product.

In conclusion, alkylation of 2-mercaptobenzothiazole with 1-(iodomethyl)-1,1,3,3,3-pentamethyl- and 1,3-bis(iodomethyl)-1,1,3,3-tetramethyldisiloxanes both in the absence and presence of the bases selectively occurs at the mercapto group to furnish first siloxane derivatives of captax. Base-free reaction of 2-mercaptobenzothiazole with 1-(iodomethyl)-1,1,3,3,3-pentamethylsiloxane is accompanied by cleavage of the Si–O bond in S-alkylation adduct with the subsequent condensation of the silanols and iodosilanes thus formed.

The study of the structures of the compounds obtained was conducted using the equipment of Baikal Analytical Center for Collective Use SB RAS.

‡ *Reaction of* **1** *with* **2** *or* **5** *in the presence of* K_2CO_3 *(general procedure).* 1 N aqueous solution of K_2CO_3 (pH 8) was added to a solution of 2-mercaptobenzothiazole **1** (0.2 g, 1.2 mmol) in acetone (20 ml). Then a solution of iodomethyldisiloxane **2** (0.35 g, 1.2 mmol) or **5** (0.25 g, 0.6 mmol) in acetone (5 ml) was added dropwise, and the mixture was refluxed for 3 h. In the case of **2**, the aqueous layer was removed and extracted with diethyl ether (2×5 ml). The extracts were combined with the organic layer and dried over $CaCl_2$. The solvent was removed under reduced pressure and the residue was distilled *in vacuo* to afford product **4**. In the case of **5**, the solvents were removed, the solid residue was washed with water and diethyl ether, and dried *in vacuo* to give compound **6**.

2-{[(1,1,3,3,3-Pentamethyldisiloxanyl)methyl]sulfanyl}-1,3-benzothiazole **4**. Yield 0.34 g (87%), colourless viscous liquid with a specific smell, bp 145–150 °C (2 Torr). IR (film, ν/cm^{-1}): 1059 (Si–O–Si). ^1H NMR (acetone-d_6) δ: 0.14 (s, 9 H, Me), 0.27 (s, 6 H, Me), 2.68 (s, 2 H, CH_2S), 7.32 (dd, H^4, $^3J_{HH}$ 8.2, 8.6 Hz), 7.42 (dd, H^8, $^3J_{HH}$ 8.4, 8.6 Hz), 7.46 (d, H^9, $^3J_{HH}$ 8.4 Hz), 7.81 (d, H^4, $^3J_{HH}$ 8.2 Hz). ^{13}C NMR (acetone-d_6) δ: –0.28 (Me), 1.19 (Me), 19.57 (CH_2), 121.24 (C^4), 124.15 ($C^{5,6}$), 126.16 (C^7), 135.38 (C^8), 153.76 (C^9), 169.61 (SC). ^{15}N NMR (acetone-d_6) δ: –81.8. ^{29}Si NMR (acetone-d_6) δ: 3.3, 9.4. Found (%): C, 47.55; H, 6.48; N, 4.00; S, 19.49; Si, 16.84. Calc. for $C_{13}H_{21}NOS_2Si_2$ (%): C, 47.66; H, 6.46; N, 4.28; S, 19.58; Si, 17.14.

2-{[3-(1,3-Benzothiazol-2-ylsulfanyl)methyl]-1,1,3,3-tetramethyldisiloxanylmethyl}sulfanyl-1,3-benzothiazole **6**. Yield 0.27 g (90%), white powder, mp 168–170 °C. IR (KBr, ν/cm^{-1}): 1077 (Si–O–Si). ^1H NMR ($CDCl_3$) δ: 0.29 (s, 12 H, Me), 2.65 (s, 4 H, CH_2S), 7.24 (dd, H^8, $^3J_{HH}$ 8.2, 8.6 Hz), 7.36 (dd, H^8, $^3J_{HH}$ 8.4, 8.6 Hz), 7.67 (d, H^9, $^3J_{HH}$ 8.4 Hz), 7.83 (d, H^8, $^3J_{HH}$ 8.2 Hz). ^{13}C NMR ($CDCl_3$) δ: 0.50 (Me), 20.18 (CH_2), 121.44 (C^4), 124.10 (C^5), 124.70 (C^6), 126.16 (C^7), 135.43 (C^8), 153.61 (C^9), 170.31 (SC). ^{15}N NMR ($CDCl_3$) δ: –85.4. ^{29}Si NMR ($CDCl_3$) δ: 5.1. Found (%): C, 48.74; H, 4.64; N, 5.36; S, 25.89; Si, 11.34. Calc. for $C_{20}H_{24}N_2OS_4Si_2$ (%): C, 48.73; H, 4.90; N, 5.68; S, 26.02; Si, 11.40.

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