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One-pot synthesis of first imidazolophanes with dimethylene(tetramethyl)disiloxane spacers

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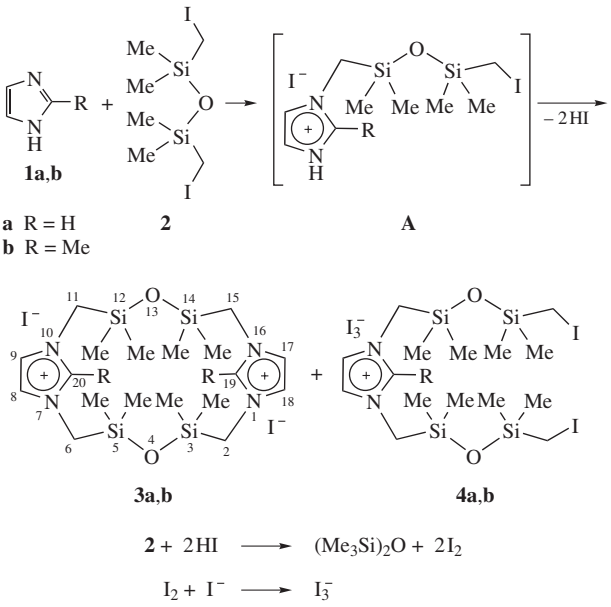
The first representative imidazolophanes bearing dimethylene(tetramethyl)disiloxane spacers were synthesized in one preparative stage by the reaction between imidazoles and 1,3-bis(iodomethyl)-1,1,3,3-tetramethyldisiloxane.

Imidazole derivatives possess diverse biological activity.[1] They constitute a core of many medicines,[2–4] environmentally benign fertilizers,[5] basic media, catalysts in organic synthesis,[6] components of mixed epoxy hardeners.[7] Siloxane-containing imidazolium iodides are promising electrochemically stable electrolytes for solar cells.[8]

The classical method for functionalization of imidazoles is based on their reaction with alkyl halides, α-haloketones, alkyl chloroformates in the presence of bases or phase transfer catalysts.[2,3,9,10] The reaction readily proceeds without catalysts if a molecule of alkylating agent contains iodomethyl moieties.[8,11]

In the present work, we report a one-pot synthesis of new functionally substituted imidazoles bearing dimethylene(tetramethyl)disiloxane fragments using catalyst- and solvent-free reaction between imidazoles **1a**,**b** and 1,3-bis(iodomethyl)-1,1,3,3-tetramethyldisiloxane **2**. The ^{1}H, ^{13}C and ^{15}N NMR monitoring of the reaction showed that alkylation is triggered by quaternization of N^{3} atom of imidazoles **1a**,**b** to afford the intermediate **A**. The latter likely participates in two parallel reactions, namely autoalkylation and alkylation with disiloxane **2**, to deliver imidazolophanes **3a**,**b** and 1,3-bis[3-(iodomethyl)-1,1,3,3-tetramethyldisiloxanyl]imidazolium triiodides **4a**,**b**, respectively (Scheme 1).†

Hydrogen iodide, formed in the course of N^{1}-alkylation, partially reduces the initial disiloxane **2** to hexamethyldisiloxane with the release of elemental iodine, which probably participates in the formation of triiodide anions of salts **4a**,**b**. According to their physical and chemical characteristics (viscous dark red oils, 1.5×10^{-3} S cm^{-1} conductivity), triiodides **4a**,**b** can be considered as new electroconducting ionic liquid.



Scheme 1

† IR spectra were recorded on a Vertex 70 spectrometer (KBr, films). ^{1}H, ^{13}C, ^{15}N and ^{29}Si NMR spectra were run on a Bruker DPX-400 instrument at 400.13, 100.61, 40.56 and 79.5 MHz, respectively. Residual protons of deuterosolvents were used as references. The UV spectra were recorded on a UV-Vis Lambda 35 spectrometer. MS study was performed by MALDI method on a Bruker Ultraflextreme III TOF/TOF instrument equipped with nitrogen laser (337 nm wavelength) using Bruker FlexControl 3.3 software in reflectron mode. MS/MS spectra were recorded in LIFT mode. The spectra were analyzed using Bruker FlexAnalysis software. NALDI™ target and MeCN or DMSO solvents were used in the experiments. The reaction course and the compounds purity were monitored by TLC (Silufol UV-254, acetone as eluent).

Reaction between compounds **1a** *and* **2**. Imidazole **1a** (0.2 g, 3 mmol) and 1,3-bis(iodomethyl)-1,1,3,3-tetramethyldisiloxane **2** (1.2 g, 3 mmol) were dissolved in acetonitrile (4 ml) upon stirring under argon flow. The solvent was removed upon heating and the homogenous mixture was stirred at 110 °C for 7 h until imidazole **1a** disappeared. The reaction products were separated by column chromatography [10×500 mm, silica gel MN Kieselgel 60 (0.063–0.2 mm), consecutive change of the eluents]. Compound **4a** was eluted with acetone, compound **3a** was eluted with methanol.

3,3,5,5,12,12,14,14-Octamethyl-4,13-dioxa-7,16-diaza-1,10-diazonia-3,5,12,14-tetrasilatricyclo[14,2,1,1^{7,10}*]icosa-1(19),8,10(20),17-tetraene diiodide* **3a**. Yield 0.25 g (24%, based on the reacted disiloxane **2**), yellow oil (R_f = 0.73, methanol). IR (film, ν/cm^{-1}): 1073 (Si–O–Si). ^{1}H NMR (CD_3OD) δ: 0.23 (s, 24H, Me), 4.08 (s, 8H, CH_2), 7.56 (s, 4H, H^{4,5}), 8.92 (s, 2H, H^{2}). ^{13}C NMR (CD_3OD) δ: –0.54 (Me), 42.97 (CH_2N), 124.85 (C^{4,5}), 135.83 (C^{2}). ^{15}N NMR (CD_3OD) δ: –206.3. ^{29}Si NMR (CD_3OD) δ: 4.9. MS (MALDI), *m*/*z*: 581 [M – I]$^{+}$. Found (%): C, 29.80; H, 4.89; I, 36.40; N, 7.64; Si, 15.36. Calc. for $C_{18}H_{38}I_2N_4O_2Si_4$ (%): C, 30.51; H, 5.40; I, 35.81; N, 7.91; Si, 15.85.

*3-Bis[(3-iodomethyl-1,1,3,3-tetramethyldisiloxanyl)methyl]-1*H*-imidazolium triiodide* **4a**. Yield 0.18 g (12%, based on the reacted disiloxane **2**), red oil (R_f = 0.84, acetone). IR (film, ν/cm^{-1}): 1064 (Si–O–Si). ^{1}H NMR (acetone-d_6) δ: 0.29 (s, 12H, Me), 0.34 (s, 12H, Me), 2.15 (s, 4H, CH_2I), 4.14 (s, 4H, CH_2), 7.68 (s, 2H, H^{4,5}), 9.00 (s, 1H, H^{2}). ^{13}C NMR (acetone-d_6) δ: –12.50 (CH_2I), –0.73 (Me), –0.51 (Me), 42.72 ($CH_2N^{1,3}$), 124.31 (C^{4,5}), 135.32 (C^{2}). ^{15}N NMR (CD_3OD) δ: –203.2. ^{29}Si NMR (CD_3OD) δ: 6.5 (NCH_2Si), 3.7 ($SiCH_2I$). MS (MALDI), *m*/*z*: 641 [M – I_3]$^{+}$. Found (%): C, 17.22; H, 3.65; I, 62.90; N, 2.79; Si, 10.15. Calc. for $C_{15}H_{35}I_5N_2O_2Si_4$ (%): C, 17.62; H, 3.45; I, 62.07; N, 2.74; Si, 10.99.

In the case of 2-methylimidazole **1b** containing the donor substituent, the yield of cyclophane is higher (34%). The reaction proceeds under similar conditions for 5 h. Cyclophane **3b** is easily precipitated from acetone solution of the reaction mixture. The acetone-soluble liquid salt **4b** can be purified by the column chromatography.

Structures of the synthesized imidazolophanes **3a**,**b** and ionic liquids **4a**,**b** were proved by elemental analysis and IR, UV, ^{1}H, ^{13}C, ^{15}N, ^{29}Si NMR and MS techniques. In the 2D ^{15}N NMR spectra of compounds **3a**,**b**, cross-peaks between the methylene protons and equivalent nitrogen atoms of the imidazole fragments are observed at –206.3 and –203.2 ppm, which confirms the cyclic structure of these compounds.

The ^{13}C NMR spectra of ionic liquids **4a**,**b** exhibit signals of carbon atoms of the terminal iodomethyl moieties at –13.23 and –13.29 ppm, respectively. Their ^{29}Si NMR spectra contain two signals at 3.7 and 6.5 ppm (**4a**), 4.3 and 6.9 ppm (**4b**) for $SiCH_2I$ and NCH_2Si fragments, respectively. In the 2D ^{15}N NMR spectra of compounds **4a**,**b**, the cross-peaks between the methylene protons and imidazole nitrogen atoms appear at –203.2 (**4a**) and –210.5 ppm (**4b**). In the UV spectra of triiodides **4a**,**b**, the absorption bands typical of (I_3^-) anion[12] are observed at 291 and 361 nm (**4a**) and 293 and 362 nm (**4b**).

In conclusion, the presence of two iodomethyl groups in the structure of siloxane allows several reactive centers to be involved into the reaction thus promoting the formation of hitherto unknown imidazolophanes in one preparative stage. This opens an access to novel families of cyclophanes bearing dimethylene-(tetramethyl)disiloxane spacers, which seem to be promising building blocks for the design of receptors and sensors with specific properties,[13] molecular containers and catalysts,[14] ionic liquids,[15] antibiotic and antitumor drugs.[16]

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Reaction between compounds **1b** *and* **2**. 2-Methylimidazole **1b** (0.3 g, 3.6 mmol) and 1,3-bis(iodomethyl)-1,1,3,3-tetramethyldisiloxane **2** (1.5 g, 3.6 mmol) were dissolved in acetonitrile (5 ml) upon stirring under argon flow. The solvent was removed upon heating and homogeneous mixture was stirred at 150 °C for 8 h until imidazole **1b** disappeared. The reaction mixture was dissolved in acetone (20 ml). The residue formed **3b** was filtered off, dried, and purified by precipitation with diethyl ether (30 ml) from the methanol solution (5 ml). The acetone-soluble residue was purified by column chromatography [10×500 mm, silica gel MN Kieselgel 60 (0.063–0.2 mm), acetone as eluent].

3,3,5,5,12,12,14,14,19,20-Decamethyl-4,13-dioxa-7,16-diaza-1,10-diazonia-3,5,12,14-tetrasilatricyclo[14,2,1,1^{7,10}*]icosa-1(19),8,10(20),17-tetraene diiodide* **3b**. Yield 0.46 g (34%, based on the reacted disiloxane **2**), white crystals, mp 148–149 °C. IR (KBr, ν/cm^{-1}): 1059 (Si–O–Si). ^{1}H NMR (DMSO-d_6) δ: 0.17 (s, 12H, Me), 2.58 (s, 6H, Me), 3.96 (s, 8H, CH_2), 7.60 (s, 4H, H^{4,5}). ^{13}C NMR (DMSO-d_6) δ: –0.68 (SiMe), 40.23 ($CH_2N^{1,3}$), 121.79 (C^{4,5}), 142.31 (C^{2}). ^{15}N NMR (DMSO-d_6) δ: –209.8. ^{29}Si NMR (DMSO-d_6) δ: 6.5. MS (MALDI), *m*/*z*: 609 [M–I]$^+$. Found (%): C, 32.14; H, 5.54; I, 34.10; N, 7.83; Si, 15.18. Calc. for $C_{20}H_{42}I_2N_4O_2Si_4$ (%): C, 32.60; H, 5.70; I, 34.51; N, 7.60; Si, 15.21.

*1,3-Bis[(3-iodomethyl-1,1,3,3-tetramethyldisiloxanyl)methyl]-2-methyl-1*H*-imidazolium triiodide* **4b**. Yield 0.19 g (11%, based on the reacted disiloxane **2**), red oil (R_f = 0.84, acetone). IR (film, ν/cm^{-1}): 1056 (Si–O–Si). ^{1}H NMR (acetone-d_6) δ: 0.27 (s, 12H, Me), 0.29 (s, 12H, Me), 2.05 (s, 4H, CH_2I), 2.63 (s, 3H, Me_{Im}), 3.92 (s, 4H, CH_2), 7.48 (s, 2H, H^{4,5}). ^{13}C NMR (acetone-d_6) δ: –13.29 (CH_2I), –1.01 (SiMe), 11.03 (Me_{Im}), 40.10 (CH_2N), 118.98 (C^{4,5}), 144.05 (C^{2}). ^{15}N NMR (acetone-d_6) δ: –210.5. ^{29}Si NMR (CD_3OD) δ: 6.9 (NCH_2Si), 4.3 ($SiCH_2I$). MS (MALDI), *m*/*z*: 655 [M–I_3]$^+$. Found (%): C, 17.87; H, 3.15; I, 61.85; N, 3.10; Si, 11.15. Calc. for $C_{16}H_{37}I_5N_2O_2Si_4$ (%): C, 18.54; H, 3.60; I, 61.23; N, 2.70; Si, 10.84.

References

1 (*a*) M. L. Deb and P. J. Bhuyan, *Tetrahedron Lett*., 2005, **46**, 6453; (*b*) H. Wu, F. R. Zhang, Y. Wan and L. Ye, *Lett. Org. Chem.*, 2005, **5**, 209; (*c*) J. M. Xu, B. K. Liu, W. B. Wu, Q. Wu and X. F. Lin, *J. Org. Chem*., 2006, **71**, 3991; (*d*) K. Gong, D. Fang, H. L. Wang and Z. L. Liu, *Monatsh. Chem*., 2007, **138**, 1195; (*e*) L. D. S.Yadav and A. Rai, *Tetrahedron Lett*., 2009, **50**, 640.

2 (*a*) H. Matsuda, N. Fukuda, T. Ueno, M. Katakawa, X. Wang, T. Watanabe, S. Matsiu, T. Aoyama, K. Saito, T. Bando, Y. Matsumoto, H. Nagase, K. Matsumoto and H. Sugiyama, *Kidney Int*., 2011, **79**, 45; (*b*) K. Shinohara, T. Bando and H. Sugiyama, *Anticancer Drugs*, 2010, **21**, 228; (*c*) S. Kanjilal, S. Sunitha, P. S. Reddy, K. P. Kumar, U. S. N. Murty and R. B. N. Prasad, *Eur. J. Lipid Technol.*, 2009, **111**, 941; (*d*) P. C. Chan, R. C. Sills, G. E. Kissling, A. Nyska and W. Richter, *Arch. Toxicol*., 2008, **82**, 399.

3 M. P. Hay, W. R. Wilson and W. A. Denny, *Tetrahedron*, 2000, **56**, 645.

4 S. Khabnadideh, Z. Rezaei, A. Khalafi-Nezhad, R. Bahrinajafi, R. Mohamadi and A. A. Farrokhroz, *Bioorg. Med. Chem. Lett*., 2003, **13**, 2863.

5 B. C. Banerjee and S. Roy, *Indian J. Chem., Sect. B*, 2008, **47**, 1108.

6 T. Jiang, X. Ma, Y. Zhou, S. Liang, J. Zhang and B. Han, *Green Chem.*, 2008, **10**, 465.

7 A. D. Eselev and V. A. Bobylev, *Klei Germetiki Tekhnologii*, 2005, **4**, 2 (in Russian).

8 S. Lee, Y. Jeon, Y. Lim, A. Hossain, S. Lee, Y. Cho, H. Ju and W. Kim, *Electrochim. Acta*, 2013, **107**, 675.

9 A. Grimison, J. H. Ridd and B. Smith, *J. Chem. Soc.*, 1960, 1352.

10 (*a*) V. C. Casilda, E. Perez-Mayoral, M. A. Banares and E. L. Diz, *Chem. Eng. J*., 2010, **161**, 371; (*b*) C. Cernatescu and E. Comanita, *CI&CEQ*, 2005, **11**, 19; (*c*) E. Diez-Barra, A. Hoz, A. Sanchez and J. Tejeda, *Synth. Commun.*, 1993, **23**, 1783.

11 (*a*) N. O. Yarosh, L. V. Zhilitskaya, L. G. Shagun, I. A. Dorofeev, L. I. Larina and M. G. Voronkov, *Russ. J. Org. Chem*., 2013, **49**, 475 (*Zh. Org. Khim*., 2013, **49**, 486); (*b*) L. G. Shagun, I. A. Dorofeev, N. O. Yarosh, L. V. Zhilitskaya, L. I. Larina and M. G. Voronkov, *Russ. J. Org. Chem*., 2013, **49**, 1693 (*Zh. Org. Khim*., 2013, **49**, 1528).

12 P. Reiller, F. Mercier-Bion, N. Gimenez, N. Barre and F. Miserque, *Radiochim. Acta*, 2006, **94**, 739.

13 (*a*) J. Rebek, *Chem. Soc. Rev*., 1996, **25**, 255; (*b*) S. H. Gilman, *Chem. Rev*., 1997, **95**, 2529; (*c*) E. Alcalde, C. Alvarez-Rua, S. Garcia-Granda, E. Garcia-Rodriguez, N. Mesquida and L. Perez-Garcia, *Chem. Commun*., 1999, 295; (*d*) J. Yoon, S. K. Kim, N. J. Sing and K. S. Kim, *Chem. Soc. Rev*., 2006, **35**, 355.

14 D. V. Kulikov, A. A. Karasik, A. S. Balueva, O. N. Kataeva, I. A. Litvinov, E. Hey-Hawkins and O. G. Sinyashin, *Mendeleev Commun*., 2007, **17**, 195.

15 (*a*) A. D. Headley and B. Ni, *Aldrichim. Acta*, 2007, **40**, 107; (*b*) Y. Ishida, D. Sasaki, H. Miyauchi and K. Saigo, *Tetrahedron Lett*., 2006, **47**, 7973.

16 (*a*) O. V. Zvereva, A. V. Milyutin, O. V. Bobrovskaya and T. F. Odogova, *J. Pharm. Chem.*, 2004, **38**, 90; (*b*) G. Y. Ishmuratov, M. P. Yakovleva, G. R. Mingaleeva and A. G. Tolstikov, *Macroheterocycles*, 2011, **4**, 270.

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