

Polymers | Hot Paper |

BN- and BO-Doped Inorganic–Organic Hybrid Polymers with Sulfoximine Core Units

Felix Brosge⁺,^[a] Thomas Lorenz⁺,^[b] Holger Helten,^{*,[b]} and Carsten Bolm^{*,[a]}

In memory of Professor Dr. Dieter Enders

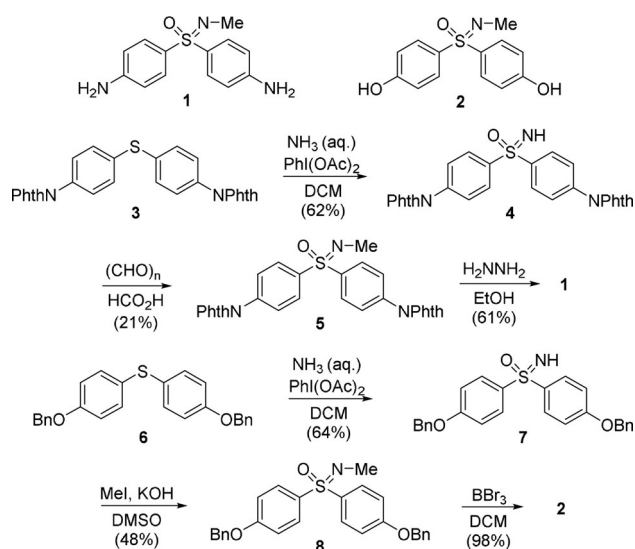
Abstract: While polysulfones constitute a class of well-established, highly valuable applied materials, knowledge about polymers based on the related sulfoximine group is very limited. We have employed functionalized diaryl sulfoximines and a *p*-phenylene bisborane as building blocks for unprecedented BN- and BO-doped alternating inorganic–organic hybrid copolymers. While the former were accessed by a facile silicon/boron exchange protocol, the synthesis of polymers with main-chain B–O linkages was achieved by salt elimination.

Polysulfones are a family of plastic materials that are noted for their high thermal and oxidative stability.^[1] They are being used within fluid handling components, steam sterilizable biomedical moldings as well as in a range of chemical process and automotive applications.^[2] Some of us recently reported a series of BN-doped inorganic–organic hybrid polymers,^[3–6] including the first poly(*p*-phenylene iminoborane), which can be regarded as a BN-analogue of poly(*p*-phenylene vinylene) (PPV).^[3d] A dapsone-type diaryl sulfone was also incorporated into a polymeric material.^[3e]

Formal exchange of a sulfonyl oxygen by a nitrogen atom converts a sulfone into a sulfoximine. The latter compounds are relevant in asymmetric synthesis^[7] and applications in medicinal^[8] and crop protection chemistry.^[9] Functionalizing the sulfoximine nitrogen allows a fine-tuning of physicochemical

properties, which proved useful in drug design and bioactivity adjustment.^[10] Surprisingly, sulfoximines have only once been applied as building blocks in polymers.^[11] In that study, Takata et al. used Friedel–Crafts reactions to prepare polysulfoximines with molecular weights (M_n) of approximately 13 000. Herein, we describe the synthesis and characterization of the first inorganic–organic hybrid polysulfoximines.

In light of previous work,^[12] sulfoximines **1** and **2** were identified as suitable organic starting materials. Both compounds were N-methylated, thereby confining the reactive anchor sites of the molecules to the free aryl amino and hydroxyl groups. With the vision to allow future variations of the N-substituent, phthalimid- and benzyl-protected NH-sulfoximines **4** and **7**, respectively, were targeted first. The synthetic sequences are shown in Scheme 1. The preparation of **1** started from known

Scheme 1. Syntheses of key intermediates **1** and **2**.

diarylsulfide **3**,^[12] which was imidated and oxidized by adopting a protocol reported by Luisi, Bull, and others^[13] to give **4** in 62% yield. Noteworthy, we applied aqueous ammonia as a nitrogen source instead of the originally suggested ammonium carbamate.

N-Methylation under standard Escheiwer–Clark conditions afforded sulfoximine **5** (21%), which was deprotected with hydrazine in ethanol to give **1** in 61% yield. Following an analogous reaction sequence, sulfoximine **2** was prepared by imida-

[a] F. Brosge,⁺ Prof. Dr. C. Bolm
Institute of Organic Chemistry, RWTH Aachen University
Landoltweg 1, 52074 Aachen (Germany)
E-mail: carsten.bolm@rwth-aachen.de

[b] T. Lorenz,⁺ Priv.-Doz. Dr. H. Helten
Institute of Inorganic Chemistry, RWTH Aachen University
Landoltweg 1, 52074 Aachen (Germany)
New address: Institute of Inorganic Chemistry,
Julius-Maximilians-Universität Würzburg
Am Hubland, 97074 Würzburg (Germany)
E-mail: holger.helten@uni-wuerzburg.de

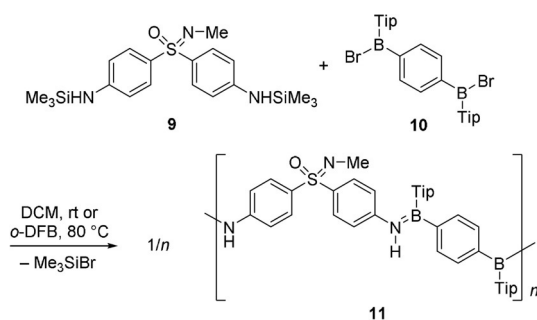
[*] These authors contributed equally.

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under:
<https://doi.org/10.1002/chem.201903289>.

© 2019 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

tion/oxidation of **6**^[14] to give **7** (64%) followed by N-methylation with MeI in KOH/DMSO^[15] providing **8** in 48% yield and sequential debenzoylation with BBr₃ (98%).

Targeting a polymer formation by silicon/boron exchange, bis(silylated) sulfoximine **9** was prepared, in analogy of literature precedence,^[16] by treatment of **1** with a mixture of Me₃SiCl and Et₃N in THF at 45 °C for 24 h. The coupling partner for **9** was bis(bromoborane) **10**^[3d] (Tip = 2,4,6-triisopropylphenyl). Two co-polycondensation reactions were performed (Scheme 2). In both cases, a 1:1 ratio of **9** and **10** was applied.



Scheme 2. Polycondensation reaction of sulfoximine **9** and bisborane **10** to give alternating copolymer **11**.

In the first experiment (trial 1), the mixture was kept in dichloromethane for 3 days at ambient temperature. Trial 2 involved *o*-difluorobenzene (*o*-DFB) as the solvent and heating the mixture to 80 °C for 24 h. The resulting alternating copolymers **11** were then purified by precipitation from concentrated solution with hexane and subsequent drying in vacuo. The identities of copolymers **11**, which were obtained as off-white solids, were unambiguously ascertained by NMR spectroscopy. Their molecular mass distributions were determined by gel permeation chromatography (GPC, Table 1). For both samples, the ¹H NMR spectrum showed a shift of the NH-Signal from $\delta = 3.77$ ppm in **9** to the aromatic region in **11** ($\delta = 7.25$ ppm), which was also observed in previously prepared related BN polymers.^[3d]

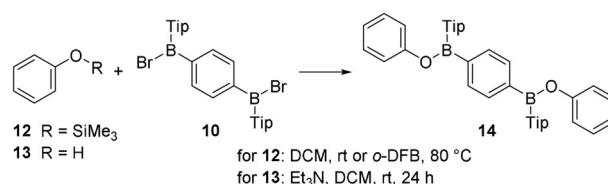
Table 1. GPC data of polymers **11** and **15** (against polystyrene standards).

	M_n	M_w	PDI	DP_n
11 (trial 1) ^[a]	9 750	18 600	1.91	13
11 (trial 2) ^[b]	11 830	28 900	2.44	15
15 (trial 1) ^[a]	2400	2970	1.52	3
15 (trial 2) ^[b]	5300	9740	1.84	7

[a] Prepared in dichloromethane (DCM), rt, 3 d. [b] Prepared in *o*-difluorobenzene (*o*-DFB), 80 °C, 24 h.

The GPC analyses revealed number average molecular weights of $M_n = 9\,750$ (trial 1) and $11\,830$ (trial 2), according to polymerization degrees of $DP_n = 13$ and 15 , respectively. The polydispersity indices were close to 2, as expected for step-growth polycondensation processes.

Next, copolymers with main-chain B–O linkages^[17] were targeted. Hypothesizing that such products could be accessed by analogous Si/B exchange reactions as applied before in the synthesis of **11**, organic starting materials with silylated phenolic hydroxyl groups became of interest. In order to get an estimate of the feasibility of such an approach, a prior model reaction between **10** and trimethylsilylated phenol **12** was performed (Scheme 3). In the first experiment, the reaction was



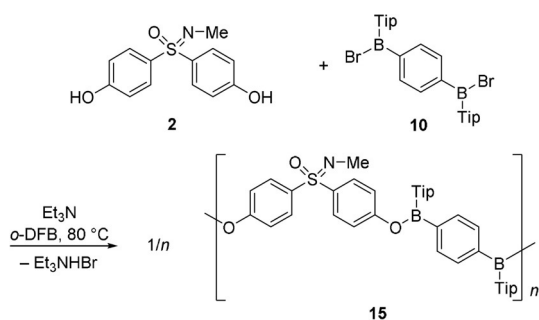
Scheme 3. Model reactions testing the feasibility of Si/B exchange and salt elimination reactions in the formation of alternating copolymers with B–O linkages.

run in dichloromethane at room temperature. As hypothesized, product **14** was indeed formed as revealed by ¹H and ¹¹B NMR spectroscopy. The initial presence of two doublets ($\delta = 8.04$ and 7.88 ppm) in the ¹H NMR spectrum suggested a stepwise formation of **14**. However, the entire process was very slow, and even after four weeks the conversion was not yet complete. A similar outcome resulted when *o*-difluorobenzene was used as a solvent at a reaction temperature of 80 °C. Also in this case, the conversion was slow, taking five weeks in total. Although these results showed that a Si/B exchange could, in principle, be applied to accomplish a B–O bond formation starting from **10**, the slow rate of this process proved unfavorable for its application to co-polycondensation reactions. Therefore, we decided to investigate B–O bond formation between **10** and the parent free phenol (**13**).

While initial attempts without base remained unsatisfying, the presence of triethylamine had a tremendously positive effect, leading to a clean and quantitative coupling providing **14** within 24 hours at room temperature. Compound **14** was then isolated by filtration and characterized by multinuclear NMR spectroscopy. The ¹¹B{¹H} NMR spectrum showed a resonance at $\delta = 47.3$ ppm, which is in the expected range for the suggested constitution.

Encouraged by this result, the aforementioned conditions were applied in the copolymerization of sulfoximine **2** with bisborane **10** (Scheme 4). Within three days in the presence of Et₃N, the dichloromethane solution became highly viscous (trial 1). However, after work-up the GPC analysis revealed that the product was of relatively low molecular weight ($M_n = 2\,400$, $DP_n = 3$; Table 1). Consequently, in the next experiment (trial 2) the solvent was changed to *o*-DFB, and then the reaction temperature was raised to 80 °C. Pleasingly, in this manner, after 24 h the molecular weight (M_n) of the resulting polymer **15** was increased to $5\,300$, revealing an average chain length of $DP_n = 7$ (Table 1).^[18]

In summary, we have prepared the first inorganic–organic hybrid sulfoximine-containing polymers as alternating copoly-



Scheme 4. Polycondensation reaction of sulfoximine **2** and bisborane **10** to give alternating copolymer **15**.

mers with B=N and B–O linkages. While our Si/B exchange polycondensation protocol was successful in the former case, for the synthesis of polymers with B–O linkages in the main chain a salt elimination approach proved to be favorable. In view of the recently demonstrated advantageous effect of the formulation of dapson-type drugs into polymer conjugates for anti-inflammatory purposes^[19] on the one hand, and the well-established biomedical activity of many boron-containing polymers^[20] on the other hand, we are currently exploring the biomedical potential of our novel sulfoximine-B=N/B–O hybrids in detail.

Acknowledgements

H. Helten thanks the German Research Foundation (DFG) for funding through the Heisenberg Programme (HE 6171/7-1, 401738081), the Research Grant HE 6171/6-1 (401739196), and Prof. Dr. Jun Okuda for his generous support and valuable advice.

Conflict of interest

The authors declare no conflict of interest.

Keywords: boron · hybrid materials · polymers · sulfoximines · sulfur

- [1] J. B. Rose, *Polymer* **1974**, *15*, 456–465.
 [2] D. Parker, J. Bussink, H. T. van de Grampel, G. W. Wheatley, E. Dorf, E. Ostlinning, K. Reinking (Eds.) *Polymers, High Temperature*. In *Ullmann's Encyclopedia of Industrial Chemistry* **2000**.
 [3] a) T. Lorenz, A. Lik, F. A. Plamper, H. Helten, *Angew. Chem. Int. Ed.* **2016**, *55*, 7236–7241; *Angew. Chem.* **2016**, *128*, 7352–7357; b) O. Ayhan, T. Eckert, F. A. Plamper, H. Helten, *Angew. Chem. Int. Ed.* **2016**, *55*, 13321–13325; *Angew. Chem.* **2016**, *128*, 13515–13519; c) concept: H. Helten, *Chem. Eur. J.* **2016**, *22*, 12972–12982; d) T. Lorenz, M. Crumbach, T. Eckert, A. Lik, H. Helten, *Angew. Chem. Int. Ed.* **2017**, *56*, 2780–2784; *Angew. Chem.* **2017**, *129*, 2824–2828; e) N. A. Riensch, A. Deniz, S. Kühl, L. Müller, A. Adams, A. Pich, H. Helten, *Polym. Chem.* **2017**, *8*, 5264–5268; f) O. Ayhan, N. A. Riensch, C. Glasmacher, H. Helten, *Chem. Eur. J.* **2018**, *24*, 5883–5894; g) review: H. Helten, *Chem. Asian J.* **2019**, *14*, 919–935.
 [4] Examples from other groups: a) A. W. Baggett, F. Guo, B. Li, S.-Y. Liu, F. Jäkle, *Angew. Chem. Int. Ed.* **2015**, *54*, 11191–11195; *Angew. Chem.* **2015**, *127*, 11343–11347; b) X.-Y. Wang, F.-D. Zhuang, J.-Y. Wang, J. Pei, *Chem.*

- Commun.* **2015**, *51*, 17532–17535; c) W.-M. Wan, A. W. Baggett, F. Cheng, H. Lin, S.-Y. Liu, F. Jäkle, *Chem. Commun.* **2016**, *52*, 13616–13619; d) D. Marinelli, F. Fasano, B. Najjari, N. Demitri, D. Bonifazi, *J. Am. Chem. Soc.* **2017**, *139*, 5503–5519; e) W. Zhang, G. Li, L. Xu, Y. Zhuo, W. Wan, N. Yan, G. He, *Chem. Sci.* **2018**, *9*, 4444–4450; f) H. L. van de Wouw, J. Young Lee, E. C. Awuyah, R. S. Klausen, *Angew. Chem. Int. Ed.* **2018**, *57*, 1673–1677; *Angew. Chem.* **2018**, *130*, 1689–1693.
 [5] For polymers with B–N single bond linkages, see e.g.: a) A. Staubitz, A. Presa Soto, I. Manners, *Angew. Chem. Int. Ed.* **2008**, *47*, 6212–6215; *Angew. Chem.* **2008**, *120*, 6308–6311; b) A. Staubitz, M. E. Sloan, A. P. M. Robertson, A. Friedrich, S. Schneider, P. J. Gates, J. Schmedt auf der Günne, I. Manners, *J. Am. Chem. Soc.* **2010**, *132*, 13332–13345; c) W. C. Ewing, A. Marchione, D. W. Himmelberger, P. J. Carroll, L. G. Sneddon, *J. Am. Chem. Soc.* **2011**, *133*, 17093–17099; d) A. N. Marziale, A. Friedrich, I. Klopsch, M. Drees, V. R. Celinski, J. Schmedt auf der Günne, S. Schneider, *J. Am. Chem. Soc.* **2013**, *135*, 13342–13355; e) A. P. M. Robertson, E. M. Leitao, T. Jurca, M. F. Haddow, H. Helten, G. C. Lloyd-Jones, I. Manners, *J. Am. Chem. Soc.* **2013**, *135*, 12670–12683; f) A. Kumar, H. C. Johnson, T. N. Hooper, A. S. Weler, A. G. Algarra, S. A. Macgregor, *Chem. Sci.* **2014**, *5*, 2546–2553; g) H. C. Johnson, E. M. Leitao, G. R. Whittell, I. Manners, G. C. Lloyd-Jones, A. S. Weller, *J. Am. Chem. Soc.* **2014**, *136*, 9078–9093; h) H. C. Johnson, A. S. Weller, *Angew. Chem. Int. Ed.* **2015**, *54*, 10173–10177; *Angew. Chem.* **2015**, *127*, 10311–10315; i) A. Ledoux, P. Larini, C. Boisson, V. Monteil, J. Raynaud, E. Lacôte, *Angew. Chem. Int. Ed.* **2015**, *54*, 15744–15749; *Angew. Chem.* **2015**, *127*, 15970–15975; j) F. Anke, D. Han, M. Klahn, A. Spannenberg, T. Beweries, *Dalton Trans.* **2017**, *46*, 6843–6847.
 [6] For organoborane hybrid polymers with B–C linkages, see e.g.: a) A. Lik, L. Fritze, L. Müller, H. Helten, *J. Am. Chem. Soc.* **2017**, *139*, 5692–5695; b) A. Lik, S. Jenthra, L. Fritze, L. Müller, K.-N. Truong, H. Helten, *Chem. Eur. J.* **2018**, *24*, 11961–11972.
 [7] a) H. Okamura, C. Bolm, *Chem. Lett.* **2004**, *33*, 482–487; b) T. Toru, C. Bolm, *Organosulfur Chemistry in Asymmetric Synthesis* Wiley-VCH, Weinheim, **2008**; c) V. Bizet, C. M. M. Hendriks, C. Bolm, *Chem. Soc. Rev.* **2015**, *44*, 3378–3390; d) V. Bizet, R. Kowalczyk, C. Bolm, *Chem. Soc. Rev.* **2014**, *43*, 2426–2438; e) X. Shen, J. Hu, *Eur. J. Org. Chem.* **2014**, 4437–4451; f) J. A. Bull, L. Degennaro, R. Luisi, *Synlett* **2017**, *28*, 2525–2538.
 [8] a) U. Lücking, *Angew. Chem. Int. Ed.* **2013**, *52*, 9399–3408; *Angew. Chem.* **2013**, *125*, 9570–9580; b) M. Frings, C. Bolm, A. Blum, C. Gnam, *Eur. J. Med. Chem.* **2017**, *126*, 225–245; c) U. Lücking, *Org. Chem. Front.* **2019**, *6*, 1319–1324.
 [9] K. E. Arndt, D. C. Bland, N. M. Irvine, S. L. Powers, T. P. Martin, J. R. McConnell, D. E. Podhoerz, J. M. Renga, R. Ross, G. A. Roth, B. D. Scherzner, T. W. Toyzan, *Org. Process. Res. Dev.* **2015**, *19*, 454–462.
 [10] a) F. W. Goldberg, J. G. Kettle, J. Xiong, D. Lin, *Tetrahedron* **2014**, *70*, 6613–6622; b) K. M. Foote, K. W. M. Nissik, T. McGuire, P. Turner, S. Guichard, J. W. T. Yates, A. Lau, K. Blades, D. Heathcote, R. Odedra, G. Wilkinson, Z. Wilson, C. M. Wood, P. J. Jewsbury, *J. Med. Chem.* **2018**, *61*, 9889–9907.
 [11] T. Takata, K. Namakura, T. Endo, *Macromolecules* **1996**, *29*, 2696–2697.
 [12] a) X. Y. Chen, H. Buschmann, C. Bolm, *Synlett* **2012**, *23*, 2808–2810; b) G. Karpel-Massler, R. E. Kast, M. D. Siegelin, A. Dwucet, E. Schneider, M.-A. Westhoff, C. R. Wirtz, X. Y. Chen, M.-E. Halatsch, C. Bolm, *Neurochem. Res.* **2017**, *42*, 3382–3389.
 [13] a) A. Tota, M. Zenzola, S. J. Chawner, S. St John-Campbell, C. Carlucci, G. Romanazzi, L. Degennaro, J. A. Bull, R. Luisi, *Chem. Commun.* **2017**, *53*, 348–351; b) J.-F. Lohier, T. Glachet, H. Marzag, A.-C. Gaumont, V. Reboul, *Chem. Commun.* **2017**, *53*, 2064–2067; c) Y. Xie, B. Zhou, S. Zhou, S. Zhou, W. Wei, J. Liu, Y. Zhang, D. Cheng, M. Chen, Y. Li, B. Wang, X.-S. Xue, Z. Li, *ChemistrySelect* **2017**, *2*, 1620–1624; d) T. Glachet, X. Franck, V. Reboul, *Synthesis* **2019**, *51*, 971–975.
 [14] K. H. V. Reddy, V. P. Reddy, J. Shanar, B. Madhav, B. S. P. A. Kumar, Y. V. D. Nageswar, *Tetrahedron Lett.* **2011**, *52*, 2679–2682.
 [15] C. M. M. Hendriks, R. A. Bohmann, M. Bohlem, C. Bolm, *Adv. Synth. Catal.* **2014**, *356*, 1847–1852.
 [16] X. Lin, Z. Zhang, L. Chen, F. Zeng, Y. Luo, X. Xu, *J. Organomet. Chem.* **2014**, *749*, 251–254.
 [17] For polymers with B–O linkages, see: a) W. Niu, M. D. Smith, J. J. Lavigne, *J. Am. Chem. Soc.* **2006**, *128*, 16466–16467; b) N. Christinat, E. Croisier, R. Scopelliti, M. Cascella, U. Röthlisberger, K. Severin, *Eur. J.*

- Inorg. Chem.* **2007**, 5177–5181; c) W. Liu, M. Pink, D. Lee, *J. Am. Chem. Soc.* **2009**, 131, 8703–8707.
- [18] The product obtained still contained some amount of [Et₃NH]Br by-product, which could not be fully separated after repeated precipitation.
- [19] L. Rojo, M. Fernandez-Gutierrez, S. Deb, M. M. Stevens, J. San Roman, *Acta Biomater.* **2015**, 27, 32–41.
- [20] J. N. Cambre, B. S. Sumerlin, *Polymer* **2011**, 52, 4631–4643.

Manuscript received: July 18, 2019
Revised manuscript received: August 20, 2019
Accepted manuscript online: August 21, 2019
Version of record online: September 9, 2019
