

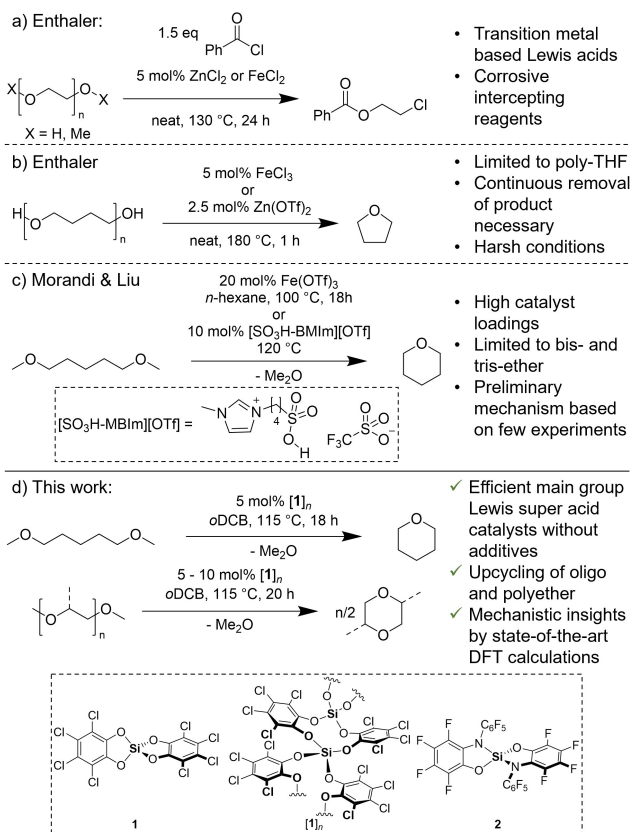
## Metathesis Reactions

## Silicon Catalyzed C–O Bond Ring Closing Metathesis of Polyethers

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**Abstract:** The Lewis superacid bis(perchlorocatecholato)silane catalyzes C–O bond metathesis of alkyl ethers with an efficiency outperforming all earlier reported systems. Chemoselective ring contractions of macrocyclic crown ethers enable substrate-specific transformations, and an unprecedented ring-closing metathesis of polyethylene glycols allows polymer-selective degradation. Quantum chemical computations scrutinize a high Lewis acidity paired with a simultaneous low propensity for polydentate substrate binding as critical for successful catalysis. Based on these mechanistic insights, a second-generation class of silicon Lewis superacid with enhanced efficacy is identified and demonstrated.

Metathesis reactions of molecules with double or triple bonds represent core technologies in organic synthesis and the chemical industry.<sup>[1]</sup> Ring-closing metatheses (RCM) of alkenes or alkynes are particularly prominent examples.<sup>[2]</sup> In contrast, catalytic metathesis reactions of singly-bonded functionalities are less explored.<sup>[3]</sup> Several examples of C–X bond metatheses relying on reversible oxidative addition of C(sp<sup>2</sup>)–X bonds have been reported.<sup>[4]</sup> However, the metathesis of C(sp<sup>3</sup>)–X bonds by oxidative addition is hampered by high barriers and possible side reactions of the alkyl intermediates (e.g.,  $\beta$ -hydride elimination).<sup>[5]</sup> Instead, Lewis acid catalysis transpired as a suitable alternative for this type of transformation.<sup>[3a,b,6]</sup> The group of Enthaler pioneered the depolymerization of polyethers by using transition metal-based Lewis acids (Figure 1a).<sup>[7]</sup> However, stoichiometric amounts of corrosive intercepting reagents such as acyl chlorides were required for sufficient conversions. Similar strategies were reported by Cantat with B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> as the catalyst, requiring excess hydrosilane to propel the



**Figure 1.** Previously reported Lewis acid catalyzed degradations of ethers. a) Lewis acid catalyzed degradation of polyethers with stoichiometric acyl chloride, b) Lewis acid catalyzed ring-closing metathesis (RCM) of polytetrahydrofuran, c) C–O bond metathesis of bi-ethers, d) RCM in bis- and polyethers catalyzed by main group Lewis superacids **1** and **2** demonstrated in this work.

reaction.<sup>[8]</sup> It was also the group of Enthaler that observed a ring-closing C–O bond metathesis from polytetrahydrofuran (Figure 1b).<sup>[9]</sup> Harsh reaction conditions and the continuous removal of THF through distillation limited this process to the less prevalent polytetrahydrofuran.<sup>[10]</sup> In 2018, Morandi et al. extended the ring-closing C–O bond metathesis to bis- and tris-ethers.<sup>[11]</sup> Using 20 mol% of Fe(OTf)<sub>3</sub>, a variety of tetrahydropyrans, tetrahydrofurans, 1,4-dioxane and morpholine derivatives were formed from the respective linear dimethoxy alkanes at elevated temperatures (Figure 1c). A comparison with other Lewis acids revealed Fe(OTf)<sub>3</sub> as the most active catalyst. Two years later, Liu et al. implemented a biphasic system consisting of the neat ether substrates and 10 mol% of the ionic liquid 1-butylsulfonate-3-methylimidazolium trifluoromethane sulfonate ([SO<sub>3</sub>H-BMIIm][OTf]) (Figure 1c).<sup>[12]</sup> Jutzi's unique silicon(II) cation Cp\*Si<sup>+</sup>

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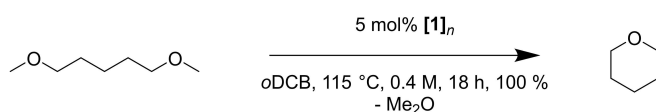
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has also catalyzed related processes.<sup>[13]</sup> All these transformations were proposed to follow a mechanism supported by some experimental observations, but a deeper understanding is pending.<sup>[11,12]</sup> Beyond, the extension of C–O bond metathesis towards polyethers, including polyethylene glycol (PEG), remains an open challenge.

The present study describes the implementation of the donor-free  $[1]_n$ -polymer of Lewis superacid bis(perchlorocatecholato)silane **1** as a catalyst for C–O bond metathesis (Figure 1d).<sup>[14]</sup> Mechanistic insights by quantum chemical calculations rationalize the outstanding efficacy of **1**. Most critical is the immunity towards chelation-deactivation by polyethers that unlocks potential recycling strategies of the pervasive PEG. Based on these findings, the design of a second-generation class of silicon(IV) based Lewis superacid catalyst is guided.

We launched our study by testing the catalytic potential of **1** in the previously reported benchmark reaction by Morandi et al., namely the C–O bond metathesis in 1,5-dimethoxypentane.<sup>[11]</sup> While a maximum of 85 % yield of the reaction product tetrahydropyran was reported with 20 mol% of Fe(OTf)<sub>3</sub> at 100 °C, only 5 mol% of  $[1]_n$  were sufficient to achieve complete conversion (Scheme 1).<sup>[11]</sup>

Diglyme (bis(2-methoxyethyl) ether) was chosen as the following model for C–O bond metathesis of substrates amenable for potential chelating-deactivation of the catalyst (Table 1). For this more challenging substrate, 50 mol% of Fe(OTf)<sub>3</sub> have been required to observe a 75 % yield of the product by GC analysis.<sup>[11]</sup> Remarkably, only 10 mol% of



**Scheme 1.** Reaction scheme of the Lewis acid catalyzed selective degradation of 1,5-dimethoxypentane to THP.

**Table 1:** Reaction optimization of the Lewis acid catalyzed C–O bond metathesis in diglyme.

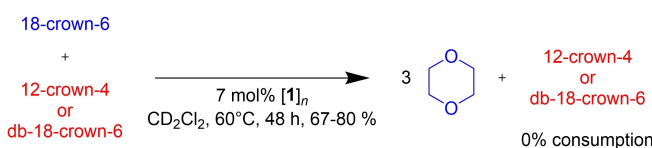
Entry	Deviations from the standard conditions	Yield [%] <sup>[a]</sup>
1	none	> 95
2	5 mol% instead of 10 mol%	43
3	5 mol%, oDFB instead of oDCB	75
4	5 mol%, DCM, Br–Ph or hexanes instead of oDCB, 60–115 °C <sup>[b]</sup>	5–29
5	5 mol%, 1-(sulfolane) <sub>2</sub> instead of $[1]_n$ , 3 d	58
6	5 mol%, Ge(cat <sup>c</sup> ) <sub>2</sub> -(sulfolane) <sub>2</sub> instead of $[1]_n$ , 3 d	40
7	5 mol%, AlCl <sub>3</sub> instead of $[1]_n$	3
8	5 mol%, B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> instead of $[1]_n$	36
9	5 mol% Fe(OTf) <sub>3</sub>	33

[a] Yields were determined by <sup>1</sup>H- and <sup>13</sup>C NMR spectroscopy using cyclooctane as an internal standard. [b] See Supporting Information for details.

$[1]_n$  afforded 1,4-dioxane in almost quantitative yield as the reaction product. Dimethyl ether as the stoichiometric side product was observed by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy using J. Young NMR tubes as reaction vessels. To edge the reactivity of **1**, several changes to the reaction parameters were evaluated (Table 1). Lowering the catalyst loading to 5 mol% still yielded a reasonable conversion of 43 % (Table 1, entry 2). Non-coordinating solvents of different polarities were investigated, indicating that higher yields are obtained in more polar solvents (Table entries 3–4). Significantly improved yields were observed with oDFB as a solvent (entry 3), but oDCB was preferred due to a boiling point stronger distinguished from the product 1,4-dioxane. The bis(sulfolane)adduct of **1** was exhibiting a lower TOF (slower reaction rate) while showing a higher TON (higher conversion, 58 %) in comparison to  $[1]_n$  (Table 1, entry 5).<sup>[15]</sup> Notably, for  $[1]_n$  as the catalyst, the activity ceases after >15 hours at elevated temperatures in the investigated reactions. We reasoned that sulfolane stabilizes the catalyst against alternative decomposition channels but lowers the TOF by competing with substrate coordination. The germanium-based analog to **1** showed a diminished TOF compared to the 1-(sulfolane)<sub>2</sub> (Table 1, entry 6).<sup>[16]</sup> AlCl<sub>3</sub> as a catalyst showed only poor performance, while with B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>, a yield of 36 % was achieved (entries 7/8). Interestingly, with 5 mol% of Fe(OTf)<sub>3</sub>, 33 % yield was obtained under our conditions (Table 1, entry 9). Still, silicon-based catalyst **1** stood out as the most active for reasons that will be explained later.

Excitingly, cyclization of a nitrogen-containing starting material into a tosyl-protected morpholine derivative also occurred quantitatively with 5 mol% of  $[1]_n$  at 60 °C, indicating an extendable substrate scope (see Supporting Information, section 1.6). Next, we investigated whether highly coordinating polyethers can be converted. Indeed, cyclic crown-ethers like 18-crown-6, 15-crown-5 and 12-crown-4 were selectively degraded to 1,4-dioxane or 2,3-dihydrobenzo[*b*][1,4]dioxine in the case of mono-benzo-18-crown-6. Catalyst loadings of 7 mol% were sufficient for quantitative conversions (for details, see Supporting Information). The bis-benzannulated derivative dibenzo(db)-18-crown-6 was not consumed in the reaction for reasons discussed in the Supporting Information (S3.3). Strikingly, the varying reaction rates allowed the selective degradation of 18-crown-6 in the presence of 12-crown-4 or db-18-crown-6 (Scheme 2). This chemoselectivity represents an attractive new way to influence the distribution and recognition patterns of these prevalent supramolecular sensors.

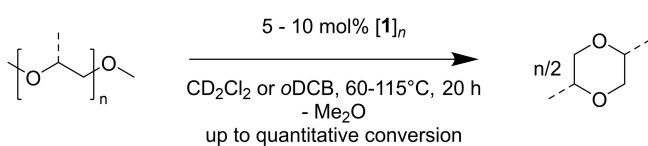
Finally, polyethylene glycol (PEG) and polypropylene glycol (PPG) were probed as substrates omnipresent in



**Scheme 2.** Competition experiment of 18-crown-6 and equimolar amounts of other crown ethers.

everyday products, cosmetics and pharmaceuticals. Depolymerization of polyethers states a field of paramount environmental interest that would establish new handles for a circular economy of these polymers.<sup>[17]</sup> Methylated derivatives of PEG and PPG with an average molecular weight of  $2000 \text{ g mol}^{-1}$  ( $n=23\text{--}46$ ) were evaluated (Scheme 3).

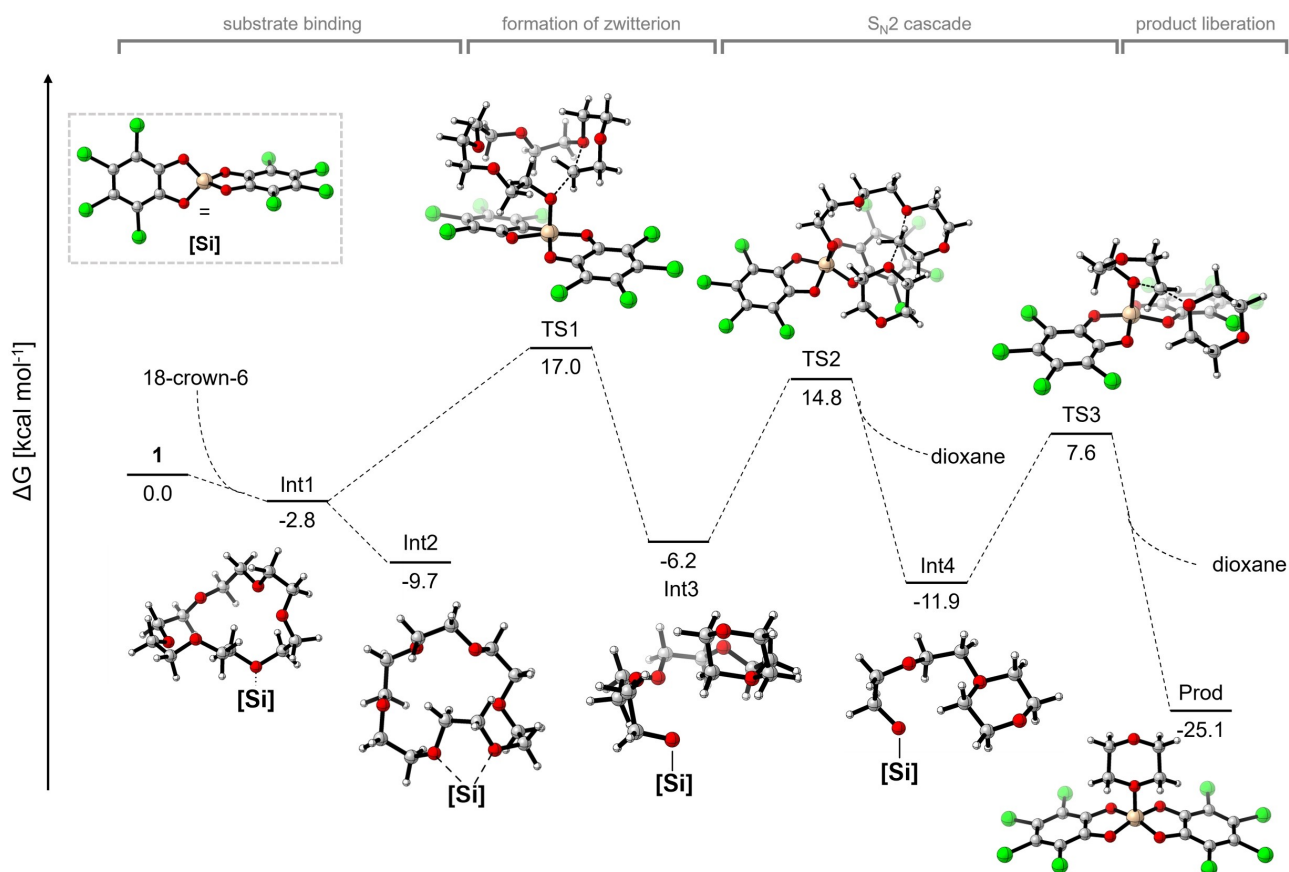
Indeed, different concentrations of PEG in *o*DCB with 10 mol% of **[1]<sub>n</sub>** showed a selective degradation of the polymer to 1,4-dioxane in quantitative yields. Interestingly, the selective decomposition of PEG in the presence of polystyrene was also achieved, giving rise to novel chemical separation strategies for these giga-ton materials (see Supporting Information). Using the same conditions in the RCM of PPG, 2,5-dimethyl-1,4-dioxane was observed as the product by NMR spectroscopy, GC MS and sXRD, though with lower conversions. Note that a C–O metathesis of secondary ethers was unsuccessful with  $\text{Fe}(\text{OTf})_3$ .<sup>[11]</sup>



**Scheme 3.** Reaction scheme of the Lewis acid catalyzed selective ring closing C–O bond metathesis of PEG and PPG.

In experiments with higher concentrations of PEG (6 wt %), an interesting side effect was noticed. While the starting PEG ( $M_w = \sim 2000 \text{ g mol}^{-1}$ ) is soluble in *o*DCB at room temperature, precipitation of a solid occurred after completion of the reaction. NMR spectroscopy revealed complete conversion, 1,4-dioxane as the sole product, while a comparison to the internal standard stated an incomplete yield of only 91 %. Hence, the newly formed solid can be assigned to PEG with increased chain length. Equimolar amounts of dibutyl and dioctyl ether were reacted in the presence of 10 mol% catalyst to support a possible chain exchange. Indeed, after a reaction time of 19 h, 13 % of the cross-metathesis product was observed by GC analysis (see Supporting Information, section 1.8). These unprecedented C–O bond exchanges enrich the toolbox of dynamic covalent chemistry and impart polyethers with vitrimeric properties.<sup>[18]</sup>

Intrigued by the experimental results, we aimed for a mechanistic understanding by DFT calculations at the DSD-BLYP(D3BJ)/def2-QZVPP + SMD(DCM)// $r^2$ SCAN-3c level. To limit conformational flexibility, the degradation of 18-crown-6 catalyzed by **1** was chosen to represent the general mechanism (Figure 2). The initial two steps consist of the coordination of the Lewis basic crown ether to the Lewis acid, first by mono-coordination (**Int1**) and second by forming a more stable dicoordinate *cis*-adduct (**Int2**) with **1**.



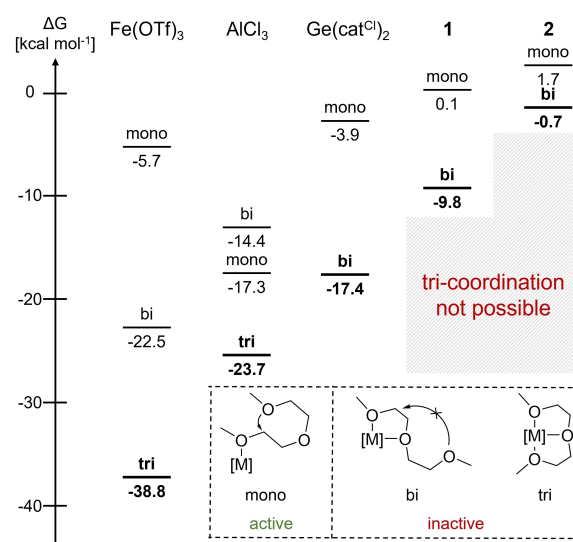
**Figure 2.** Reaction profile of the degradation of 18-crown-6 by **1** calculated at the DSD-BLYP(D3BJ)/def2-QZVPP + SMD(DCM)// $r^2$ SCAN-3c level with possible intermediates and transition states.

The nucleophilic attack by a catecholato oxygen atom of **1** on a carbon atom adjacent to the coordinated oxygen atom, as observed for group 15 catecholate-based Lewis acids,<sup>[19]</sup> would be a first putative option to launch the reaction cascade. However, an activation energy of 50 kcal mol<sup>-1</sup> renders such element ligand cooperative mode unlikely (see Supporting Information section 3.1). Instead, with an activation barrier of 26.7 kcal mol<sup>-1</sup>, the intramolecular nucleophilic attack of an oxygen atom inside the crown ether is much more plausible (**TS1**), resulting in the zwitterionic intermediate **Int3**. Despite extensive searches, a transition state with a *cis*-coordinated silicon atom was not found. From the zwitterionic intermediate **Int3**, an oxonium ion, the reaction proceeds by a cascade of intramolecular S<sub>N</sub>2 attacks on the highly polarized carbon atom with 1,4-dioxane as the leaving group. The activation energies of these steps are lower compared to the first nucleophilic attack and propelled by the release of dioxane. In the last step of the reaction, the mono-dioxane adduct of **1** is formed. This can further react with an additional molecule of 1,4-dioxane to form the respective *trans*-adduct (see ESI for scXRD), or with a molecule of 18-crown-6 to close the catalytic cycle. The exergonic binding of 1,4-dioxane explains the experimentally observed product inhibition and the required elevated processing temperature. The reaction path for the degradation of diglyme relies on the same key steps and displays similar energy barriers (see Supporting Information for details). Hence, the Lewis acid induces the reaction by polarizing the attacked carbon atom and stabilizing the resulting zwitterionic oxonium/silicate intermediate. Most important is the finding that the dicoordinated **Int2** represents a stable intermediate that would slow the overall reaction rate. Thus, mono-, bi- and tridentate binding of diglyme were analyzed for the catalysts that turned out less efficient by experiment (Figure 3, Ge(cat<sup>Cl</sup>)<sub>2</sub>, Fe(OTf)<sub>3</sub>, AlCl<sub>3</sub>). Indeed, the most active silicon Lewis acid **1** shows the slightest tendency for bidentate substrate binding.

For Fe(OTf)<sub>3</sub> and AlCl<sub>3</sub>, even the tridentate coordination is favorable and should represent an unproductive thermodynamic sink. Multidentate binding cannot be realized for B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>, explaining its second-highest activity in this catalysis.

To support these computational insights by experiment, the <sup>29</sup>Si NMR spectroscopic data of a mixture of **1** with 18-crown-6 in CD<sub>2</sub>Cl<sub>2</sub> before heating was reevaluated. Indeed, a major peak at -133.9 ppm showed the presence of hexacoordinated silicon, whereas a minor signal at -106.1 ppm revealed the partial formation of the pentacoordinate form.

This mechanistic knowledge allowed us to improve the catalytic system further. Bis(perfluoro-*N*-phenylamido phenolato)silane **2** (Figure 1d), a Lewis acid developed recently in our lab for the FLP type dihydrogen activation, was employed.<sup>[20]</sup> This Lewis acid is similarly Lewis acidic as **1**, but even less biased for bidentate substrate binding (Figure 3). Indeed, **2** exhibits a remarkably improved performance in the degradation of diglyme (3 mol%, 81%), outperforming all previous results (cf. 5 mol% of **1**, 43%).



**Figure 3.** a) Free formation enthalpies of the diglyme complexes of the herein investigated Lewis acids depending on the hapticity of the ether, calculated at the DSD-BLYP(D3BJ)/def2-QZVPP + SMD(DCM)//PBEh-3c level. The thermodynamically favored binding mode for each Lewis acid is marked in bold.

In conclusion, bis(perchlorocatecholato)silane **1** catalyzes the C–O bond metathesis reaction of polyfunctional ethers and the selective ring-closing depolymerization of polyethers (PEG and PPG). To the best of our knowledge, these transformations constitute novelties in polymer upcycling and encourage studies on process optimization for a sustainable impact on materials manufacturing and separation. The outperforming activity of **1** pinpoints the vast potential of Lewis superacids for maximum substrate activation,<sup>[21]</sup> while the low propensity for multidentate substrate-binding prevents catalyst deactivation. Based on these insights, bis(perfluoro-*N*-phenylamidophenolato)silane, a Lewis superacid immune to chelation-deactivation, is identified as an even more active catalyst.

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### Conflict of Interest

The authors declare no conflict of interest.



## Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

**Keywords:** Lewis Superacid · Organosilanes · Polyethylene Glycol · Reaction Mechanism · Ring Closing Metathesis

- [1] a) R. H. Grubbs, *Handbook of Metathesis*, Wiley-VCH, Weinheim, **2003**; b) R. H. Grubbs, S. J. Miller, G. C. Fu, *Acc. Chem. Res.* **1995**, *28*, 446–452.
- [2] a) A. Fürstner, *Angew. Chem. Int. Ed.* **2000**, *39*, 3012–3043; *Angew. Chem.* **2000**, *112*, 3140–3172; b) A. Deiters, S. F. Martin, *Chem. Rev.* **2004**, *104*, 2199–2238; c) A. Fürstner, P. W. Davies, *Chem. Commun.* **2005**, 2307–2320; d) A. H. Hoveyda, A. R. Zhugralin, *Nature* **2007**, *450*, 243–251.
- [3] a) C. M. Bell, D. A. Kissounko, S. H. Gellman, S. S. Stahl, **2007**, *46*, 761–763; b) N. A. Stephenson, J. Zhu, S. H. Gellman, S. S. Stahl, *J. Am. Chem. Soc.* **2009**, *131*, 10003–10008; c) T. Seiser, N. Cramer, *Angew. Chem. Int. Ed.* **2010**, *49*, 10163–10167; *Angew. Chem.* **2010**, *122*, 10361–10365; d) B. N. Bhawal, B. Morandi, *Angew. Chem. Int. Ed.* **2019**, *58*, 10074–10103; *Angew. Chem.* **2019**, *131*, 10178–10209; e) C. Liu, D. Chen, Y. Fu, F. Wang, J. Luo, S. Huang, *Org. Lett.* **2020**, *22*, 5701–5705.
- [4] a) J. Cornella, C. Zarate, R. Martin, *Chem. Soc. Rev.* **2014**, *43*, 8081–8097; b) Z. Lian, B. N. Bhawal, P. Yu, B. Morandi, *Science* **2017**, *356*, 1059–1063; c) S. Okumura, F. Sun, N. Ishida, M. Murakami, *J. Am. Chem. Soc.* **2017**, *139*, 12414–12417.
- [5] a) D. J. Cárdenas, *Angew. Chem. Int. Ed.* **1999**, *38*, 3018–3020; *Angew. Chem.* **1999**, *111*, 3201–3203; b) T.-Y. Luh, M.-K. Leung, K.-T. Wong, *Chem. Rev.* **2000**, *100*, 3187–3204.
- [6] Y. Ma, L. Zhang, Y. Luo, M. Nishiura, Z. Hou, *J. Am. Chem. Soc.* **2017**, *139*, 12434–12437.
- [7] a) S. Enthaler, M. Weidauer, *Chem. Eur. J.* **2012**, *18*, 1910–1913; b) S. Enthaler, M. Weidauer, *ChemSusChem* **2012**, *5*, 1195–1198; c) S. Enthaler, *Catal. Lett.* **2014**, *144*, 850–859.
- [8] E. Feghali, T. Cantat, *ChemSusChem* **2015**, *8*, 980–984.
- [9] a) S. Enthaler, A. Trautner, *ChemSusChem* **2013**, *6*, 1334–1336; b) S. Enthaler, *J. Appl. Polym. Sci.* **2014**, *131*, 39791.
- [10] Y. Wang, Y. Hou, H. Song, *Polym. Degrad. Stab.* **2017**, *144*, 17–23.
- [11] T. Biberger, S. Makai, Z. Lian, B. Morandi, *Angew. Chem. Int. Ed.* **2018**, *57*, 6940–6944; *Angew. Chem.* **2018**, *130*, 7057–7061.
- [12] H. Wang, Y. Zhao, F. Zhang, Y. Wu, R. Li, J. Xiang, Z. Wang, B. Han, Z. Liu, *Angew. Chem. Int. Ed.* **2020**, *59*, 11850–11855; *Angew. Chem.* **2020**, *132*, 11948–11953.
- [13] K. Leszczyńska, A. Mix, R. J. F. Berger, B. Rummel, B. Neumann, H.-G. Stammer, P. Jutzi, *Angew. Chem. Int. Ed.* **2011**, *50*, 6843–6846; *Angew. Chem.* **2011**, *123*, 6975–6978.
- [14] a) R. Maskey, M. Schädler, C. Legler, L. Greb, *Angew. Chem. Int. Ed.* **2018**, *57*, 1717–1720; *Angew. Chem.* **2018**, *130*, 1733–1736; b) N. Ansmann, D. Hartmann, S. Sailer, P. Erdmann, R. Maskey, M. Schorpp, L. Greb, *Angew. Chem. Int. Ed.* **2022**, *61*, e202203947; *Angew. Chem.* **2022**, *134*, e202203947.
- [15] T. Thorwart, D. Roth, L. Greb, *Chem. Eur. J.* **2021**, *27*, 10422–10427.
- [16] D. Roth, H. Wadepohl, L. Greb, *Angew. Chem. Int. Ed.* **2020**, *59*, 20930–20934; *Angew. Chem.* **2020**, *132*, 21116–21120.
- [17] a) C. Fruijtier-Pölloth, *Toxicology* **2005**, *214*, 1–38; b) A. A. D'souza, R. Shegokar, *Expert Opin. Drug Delivery* **2016**, *13*, 1257–1275.
- [18] Y. Yang, Y. Xu, Y. Ji, Y. Wei, *Prog. Mater. Sci.* **2021**, *120*, 100710.
- [19] D. Roth, J. Stirn, D. W. Stephan, L. Greb, *J. Am. Chem. Soc.* **2021**, *143*, 15845–15851.
- [20] T. Thorwart, D. Hartmann, L. Greb, *Chem. Eur. J.* **2022**, *28*, e202202273.
- [21] L. Greb, *Chem. Eur. J.* **2018**, *24*, 17881–17896.

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