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Aluminum-Catalyzed Formation of Functional 1,3,2-Dioxathiolane 2-Oxides from Sulfur Dioxide: An Easy Entry towards *N*-Substituted Aziridines

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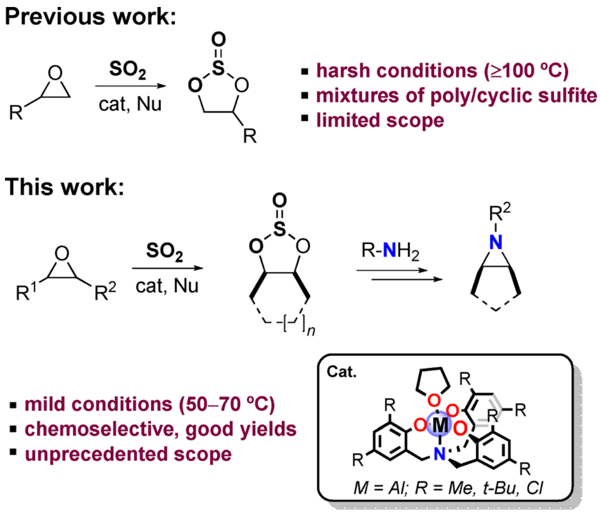
Abstract: Aluminum(III) complexes derived from aminotriphenolate ligands are shown to be excellent catalysts for the formation of cyclic sulfites from a range of (functionalized) terminal and internal epoxides, and *ex situ* generated sulfur dioxide. The developed catalytic protocol is characterized by its operational simplicity, wide scope in epoxide reaction partners, good to excellent isolated yields and mild reaction conditions [50–70 °C, $p(SO_2)$ < 1 bar]. The synthetic potential of these cyclic sulfites in organic synthesis is demonstrated in the preparation of *N*-substituted aziridines through a three-step protocol.

Keywords: aluminum; aziridines; cyclic sulfites; homogeneous catalysis; sulfur dioxide

Introduction

Small molecule catalysis and recycling has become a popular and rewarding theme in the field of organic synthesis.[1] In particular, the conversion of heterocumulenes such as carbon dioxide (CO_2),[2] carbon disulfide (CS_2)[3] and isocyanates (R–NCO)[4] has received a great deal of attention by enabling the synthesis of various heterocyclic structures. Whereas the use of CO_2 as a carbon synthon in synthesis has now become well established,[5] the use of sulfur dioxide (SO_2) as a reagent is still in its infancy.[6] One of the targeted structures that can be prepared from SO_2 are cyclic sulfites (i.e., 1,3,2-dioxathiolane 2-oxides) by coupling with epoxides (Scheme 1), providing structures of use in polymer science, as electrolyte solvents or as synthetic intermediates.[7]

The SO_2 approach has been developed as a more sustainable methodology compared to the conventional preparation of these scaffolds through a base-assisted reaction of 1,2-diols with thionyl chloride that generates stoichiometric amounts of halide-containing by-products.[8] Despite the development of various effective homogeneous and heterogeneous catalyst systems for the coupling of epoxides and SO_2,[9] there are still synthetic challenges to overcome pertinent to a more general and sustainable route towards these cyclic sulfites. In particular, low-temperature conversions and further widening the scope in reaction partners may be required to promote these cyclic sulfites as chemical building blocks. To this end, isolation of the pure sulfite targets is often hampered due to the

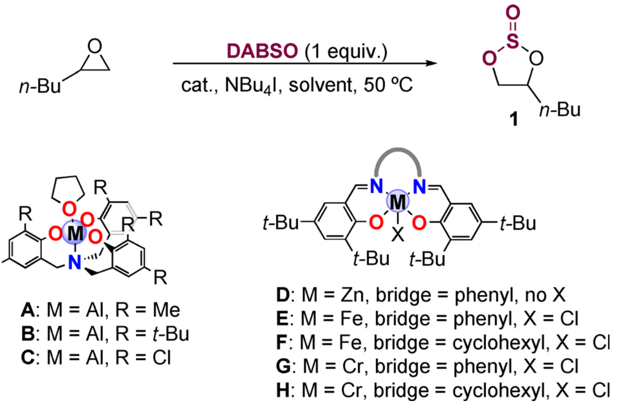


Scheme 1. Conversion of SO_2 into cyclic sulfites by reaction with epoxides: below the current approach.

presence of mixtures of poly- and cyclic sulfites. Moreover, as far as we know only limited potential towards the more challenging coupling of internal epoxides and SO_2 has been reported to date. Consequently, this restricts the synthesis of cyclic sulfites mostly to the use of terminal oxiranes.

In recent years, we have reported on the application of highly reactive and versatile aluminum(III) aminotriphenolate catalysts (Scheme 1) in the activation of terminal and internal epoxides towards the formation of various heterocyclic products[10] and polymers.[11] Inspired by these results we envisaged that these Al(III) complexes would also be potentially useful for the coupling of epoxides and SO_2 to afford cyclic sulfites, and moreover could offer a more powerful methodology towards their formation. The present contribution will show that these catalyst systems indeed show unparalleled reactivity and unusual scope in the formation of these sulfur-containing heterocycles in good to excellent isolated yields under attractively mild conditions. Furthermore, the use of these cyclic sulfites as molecular synthons is demonstrated in the preparation of *N*-substituted aziridines, which can be easily obtained through oxidation of the sulfite to a sulfate intermediate followed by subsequent aminolysis and a Wenker type base-assisted cyclization.[12]

Table 1. Screening study towards the formation of the cyclic sulfite product **1** derived from 1,2-epoxyhexane and DABSO using various catalysts and solvents.[a]



Entry	Catalyst	Solvent	*t* [h]	Yield [%][b]
1	**A**	CH_3CN	3	41
2	**B**	CH_3CN	3	51
3	**C**	CH_3CN	3	55 (63)[c]
4	**D**	CH_3CN	3	45 (49)[c]
5	**E**	CH_3CN	3	31
6	**F**	CH_3CN	3	26
7	**G**	CH_3CN	3	30
8	**H**	CH_3CN	3	47 (58)[c]
9	**C**	EtOAc	6	59
10	**C**	THF	6	23
11	**C**	DMF	6	24
12	**C**	MEK	6	19
13	–	CH_3CN	3	45

[a] *General conditions:* 3.0 mmol of 1,2-epoxyhexane, 2.5 mol% cat., 5.0 mol% NBu_4I, solvent as indicated (1 mL), 50 °C, 1 equiv. DABSO.

[b] Isolated yield.

[c] Isolated yield after a 6 h reaction time.

Results and Discussion

Our first attempts to produce cyclic sulfites from epoxides and SO_2 were based on the use of DABSO (the bis-SO_2 adduct derived from DABCO: 1,4-diazabicyclo[2.2.2]octane) as an easy to handle SO_2 surrogate,[13] see Table 1. Among the metal complexes used (*cf.*, **A–G**), the Al(III) aminotriphenolate **C**, combined with an external nucleophile (NBu_4I) to mediate the epoxide ring-opening, gave the best results in terms of isolated yield (entry 3; 55% after 3 h, 63% after 6 h). Other polar solvents beside acetonitrile were also examined but gave inferior results (entries 9–12). More importantly, the use of the nucleophilic additive only (entry 13) produced only a slightly lower yield (45%) than noted for the best case scenario (entry 3).[14] We therefore investigated the kinetic profile for the synthesis of **1** from 1,2-epoxyhexane and DABSO in more detail (Figure 1).

As can be judged from Figure 1, formation of **1** in the presence or absence of complex **C** [i.e., traces (a) and (b) in the graph] does not show much difference, and the yield of cyclic sulfite **1** reaches a plateau after around 800 min. This suggests that the Lewis acid catalytic potential of Al complex **C** is significantly hampered under these experimental conditions. The most likely reason for this lethargic behaviour is the release of the bicyclic amine DABCO during the course of the reaction when more SO_2 (DABSO) is consumed. Such diamines (and other *N*-donor Lewis bases) were found to be good ligands for Al(III) and Fe(III) aminotriphenolate complexes[15] and the presence of DABCO almost certainly causes catalyst deactivation. In order to avoid *in situ* deactivation of Al complex **C**, we designed a different protocol that takes advantage of easy SO_2 generation under practical conditions using a combination of copper powder and H_2SO_4. *Ex situ* formation of SO_2 and using a gentle and optimized nitrogen flow (see the Supporting Information for more details) to transport the SO_2 to a reactor containing the epoxide and catalyst should deliver a more productive protocol for cyclic sulfite formation. Indeed, when we probed such conditions (Table 2 and Figure 1) we noted that the reaction towards the formation of **1** proceeded more smoothly and gave the product in nearly quantitative NMR yield after only 200 min.

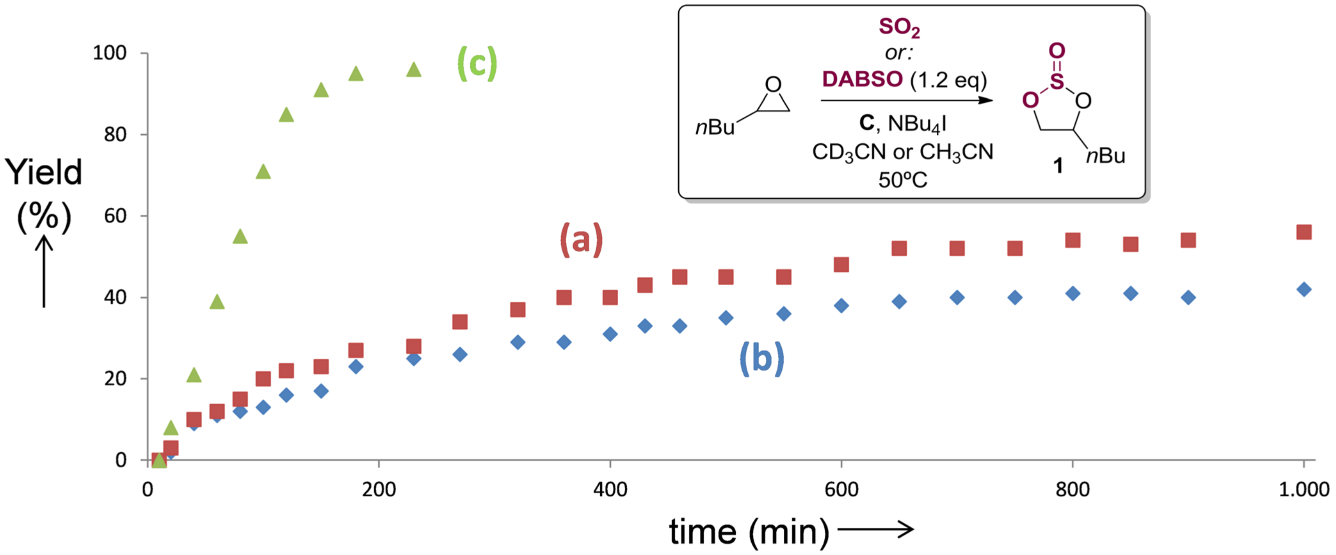


Figure 1. Kinetic profiles determined by ^{1}H NMR (CD_3CN) for the synthesis of **1** using DABSO (1.2 equiv.) and mesitylene as internal standard. (a) Using **C**/NBu_4I as binarycatalyst; (b) Only NBu_4I; (c) Reaction performed with *ex situ* generated SO_2 from H_2SO_4/Cu: epoxide (3 mmol), C (1.0 mol%), NBu_4I (2.5 mol%), CH_3CN (1.0 mL), 50 °C.

Table 2. Optimization of the protocol involving *ex situ* SO_2 formation from Cu/H_2SO_4 using catalysts **A–C**/NBu_4X and CH_3CN in the formation of the cyclic sulfite product **1**.[a]

Entry	Cat. [mol%]	Nu [mol%]	*T* [°C]	Yield [%][b]
1	–	NBu_4I (1.0)	50	11
2	–	NBu_4I (2.5)	50	29
3	–	NBu_4I (5.0)	50	61
4	–	NBu_4Br (2.5)	50	25
5	**C** (0.5)	NBu_4I (2.5)	50	85
6	**B** (0.5)	NBu_4I (2.5)	50	41
7	**A** (0.5)	NBu_4I (2.5)	50	65
8	**C** (1.0)	NBu_4I (2.5)	50	86
9	**C** (1.0)	NBu_4I (1.0)	50	61
10	**C** (0.5)	NBu_4I (2.5)	25	22
11	**C** (0.5)	NBu_4I (2.5)	70	84

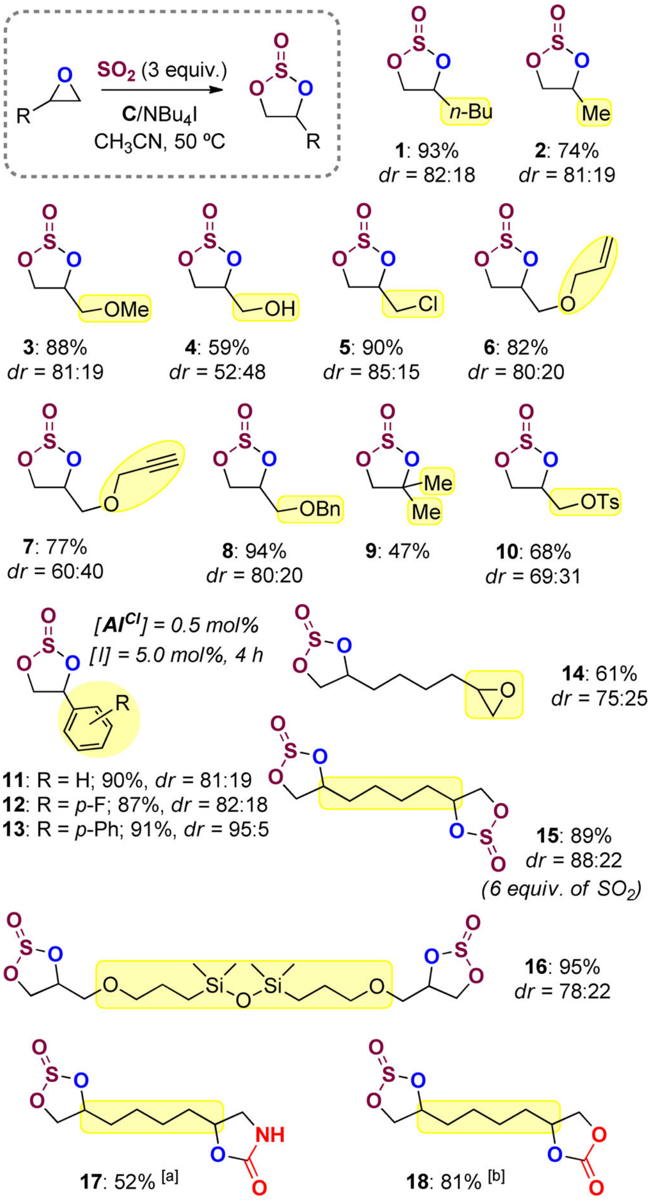
[a] *General conditions:* 3.0 mmol of 1,2-epoxyhexane, **C** (amount indicated), NBu_4X (amount indicated), CH_3CN (1 mL), Cu (3 equiv.) in H_2SO_4 (10 mL) at 90 °C (*ex situ*), 2 h.

[b] NMR yields based on mesitylene as an internal standard.

We then further optimized this improved protocol, and Table 2 summarizes the results from these experiments. Clearly, catalyst **C** shows the best performance (entries 5–7) with markedly better yields of **1** compared to the reaction in the absence of the complex (*cf.*, entries 2 *versus* 5) using a lower amount of Al complex **C** (0.5 mol%) and nucleophile (2.5 mol%). Higher amounts of Al complex (entry 8) and an elevated temperature (70 °C, entry 11) did not much affect the yield of **1**, suggesting that the conditions of entry 5 and 8 are fairly optimal.

Next we investigated the scope of terminal epoxide substrates in the formation of various cyclic sulfites (*cf.*, formation of compounds **1–18**, Figure 2) using 1.0 mol% of Al complex **C**, 2.5 mol% of NBu_4I in CH_3CN at 50 °C. Under these conditions, cyclic sulfite **1** could be isolated in excellent yield (93 %) as a mixture of two diastereoisomers in an 82:18 ratio. The presence of two diastereoisomers is the result of the non-planarity of the cyclic sulfite, with the sulfur lone pair either being on the same or opposite side of the ring substituent. The two diastereoisomers are well separated and assignable by NMR analysis (see the Supporting Information). For instance, for **1** the major isomer is characterized by three distinct signals for the hydrogens attached to the sulfite ring whereas the minor isomer shows only two peaks located at 4.52 and 4.32 ppm. The much larger difference in chemical shift for the methylene H of the ring structure ($\Delta\delta = 0.76$ ppm) in the major isomer seems to suggest that this diastereoisomer has the sulfur lone pair on the same face as the butyl substituent, thereby causing an anisotropic shift for the axial H of the methylene group. For the majority of the other cases studied similar *dr*s were noted. Fortunately, the X-ray molecular structure of cyclic sulfite **13** could be determined (Figure 3): the relative orientation of the ring substituent (*p*-biphenylene) and the sulfur lone pair is in line with the NMR observations for **1** and most of the other isolated products.[16]

Many different and potentially useful substituents on the cyclic sulfite ring can be introduced including alcohol (**4**), allyloxo (**6**), propargyloxo (**7**), and tosyl ester (**10**) groups that do not seem to hamper product formation through coordination to the Al center in **C**.[17] In those cases where styrene oxides were used (*cf.*, the formation of **11–13**), a higher loading of the



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[a] From cyclic sulfite **14**; 1.2 equiv. of phenyl carbamate, 5.0 mol% **C**, 18 h, 50 °C, CH_3CN.

[b] 0.5 mol% **C**, 2.5 mol% NBu_4I, 10 bar CO_2, 6 h, 50 °C, MEK. The *dr*s were determined by ^1H NMR.

Figure 2. Synthesis of cyclic sulfites **1–18** from various terminal epoxides using *ex situ* generated SO_2. *Conditions (unless stated otherwise):* complex **C** (1.0 mol%), NBu_4I (2.5 mol%), CH_3CN (1.0 mL), 50 °C, 3 h. Reported yields are isolated ones after column purification.

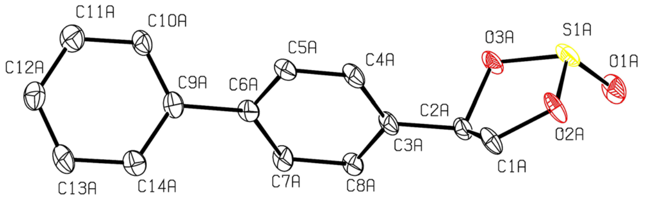


Figure 3. X-ray molecular structure for **13**. Selected bond lengths (Å) and angles (°): S(1A)–O(1) = 1.454(7), S(1A)–O(2 A) = 1.633(6), S(1A)–O(3 A) = 1.614(6); O(1A)–S(1A)–O(2A) = 105.3(4), O(1A)–S(1A)–O(3A) = 108.9(4).

nucleophile was required to prevent significant formation of ketone by-products through Meinwald rearrangement.[18] Interestingly, mono-sulfite **14** derived from its bis-epoxide precursor could be isolated in 61% yield and incorporates a synthetically useful oxirane unit. By increasing the amount of SO_2 to 6 equiv., the bis-sulfite **15** was obtained as the major compound and isolated in good yield (89%). Compound **14** could be easily converted into the mixed sulfite/carbamate **17** (52%) and sulfite/carbonate **18** (81%) by treatment with phenyl carbamate and CO_2, respectively, under appropriate reaction conditions.[10a,f] These latter conversions clearly demonstrate the post-modification potential of functional sulfites.

Motivated by the successful preparation of functional mono-substituted sulfites, we next turned our focus towards the more challenging conversion of internal epoxides. We selected cyclohexene oxide (CHO) as a representative epoxide and followed its conversion in time using the optimized conditions established for **1–18** (50 °C, 3 equiv. of SO_2, 1.0 mol% of **C**). However, NBu_4Br was utilized instead as bromide nucleophiles were previously shown to be more effective for internal epoxide conversion compared to iodide-based ones.[10a,c,e] The conversion at 50 °C proved to be a bit sluggish and, moreover, ^1H NMR analysis showed the presence of peaks reminiscent of poly-sulfites with only trace amounts of cyclic product. Therefore, the reaction between CHO and SO_2 mediated by complex **C**/NBu_4Br was then carried out at 70 °C using longer reaction times, and to our delight we found that the reaction mixture contained virtually only the cyclic sulfite product **19** (see the Supporting Information for more details). The latter was isolated in moderate yield (46%; Figure 4) by chromatographic purification. Notably, compound **19** was mostly isolated as the *trans* isomer which is the expected result if the cyclic sulfite would be formed by back-biting of an initially formed poly-sulfite polymer.[19]

Then other internal epoxides were examined as reaction partners thereby producing the cyclic sulfites **20–29** generally in appreciable yields (except for **28**; 21%). The more rigid nature of the 8-membered ring epoxide leading to cyclic sulfite **29** delivers the product in much better yield (64%) than noted for **28**; such a distinct behaviour was previously also noted in cyclic carbonate formation.[10e] The likely reason for this is the unfavourable conformation upon activation by the Al(III) center in complex **C** thereby complicating nucleophile-assisted ring-opening. The introduction of a double bond in the 8-membered ring reduces

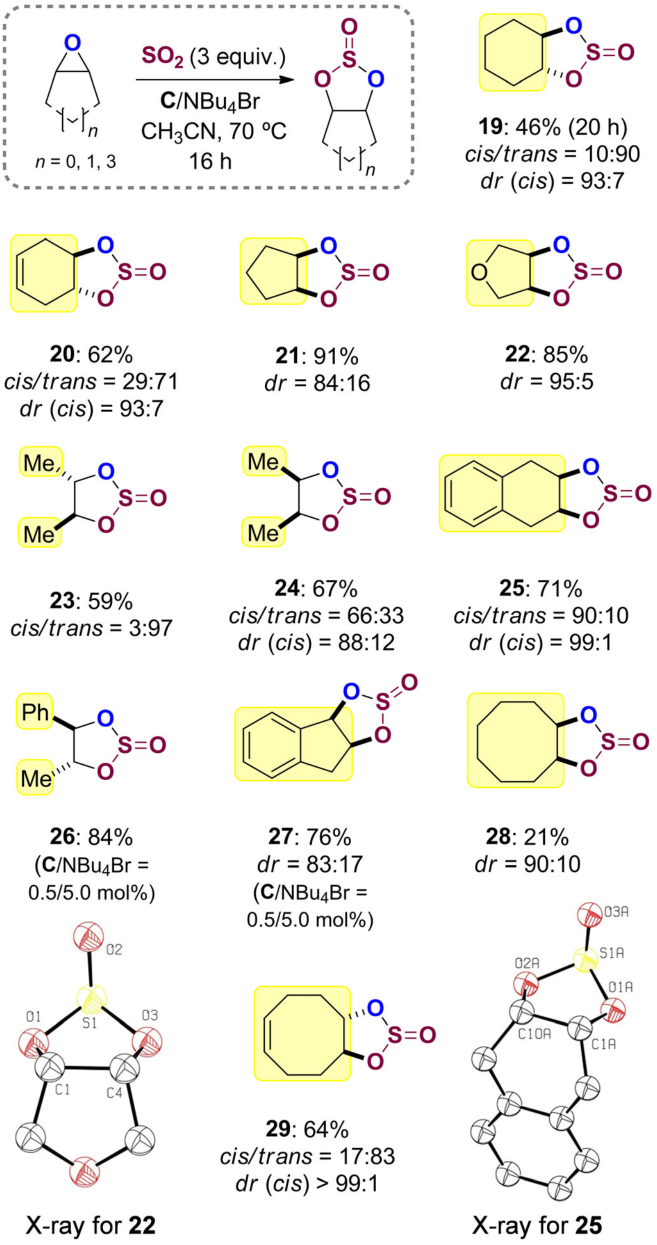


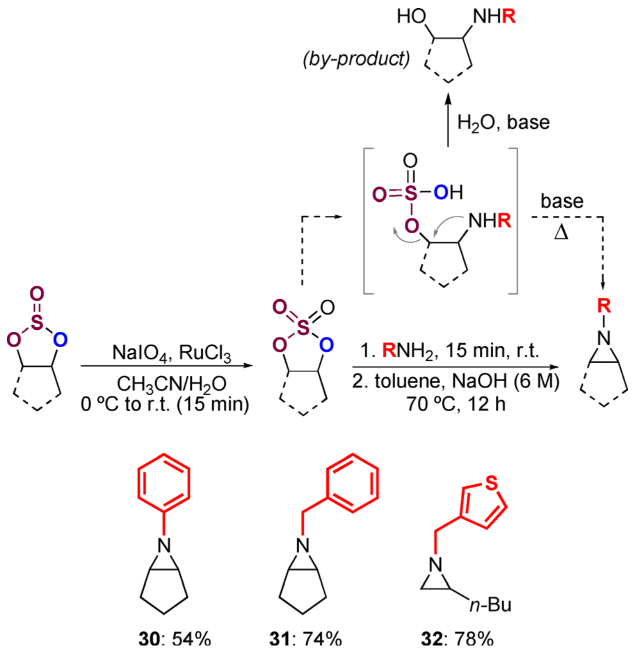
Figure 4. Synthesis of cyclic sulfites **19**–**29** from internal epoxides using *ex situ* generated SO_2. *Conditions (unless stated otherwise):* complex **C** (1.0 mol%), NBu_4Br (2.5 mol%), CH_3CN (1.0 mL), 70 °C, 16 h. Reported yields are isolated ones after column purification. The *cis*/*trans* assignments and *dr* ratios were determined by ^1H NMR. Note that for the *cis*/*trans* mixtures, only the major isomer is drawn in the Figure.

the conformational complexity and flexibility, and this should facilitate its conversion into the cyclic sulfite. The scope of products displayed in Figure 4 shows that epoxides with different ring sizes are suitable coupling partners for SO_2, and as far as we are aware our newly developed catalytic process is the first to exhibit such general potential towards the formation of cyclic sulfites from SO_2. For the conversion of *trans*-2,3-dimethyloxirane (leading to **23**) and its *cis*-isomer (giving rise to **24**) a different behaviour was noted. Whereas the *trans* substrate retains the original stereochemistry (*cis*/*trans* = 97:3), the *cis*-substrate gives rise to *cis*/*trans*-**24** with significantly lower stereo-retention indicating competing pathways leading to the formation of this product.[20]

All new compounds were completely characterized by IR/NMR spectroscopic techniques, and high-resolution mass analyses. In addition, the structures of **22** and **25** were also confirmed by X-ray analyses (Figure 4, bottom). In the determined molecular structures, the same mutual orientation of the sulfur lone pair and the cyclic sulfite ring substituents was found as revealed for **13** (Figure 3).

In order to investigate further the potential of these cyclic sulfites in organic synthesis, we considered the formation of aziridines by first oxidizing the respective sulfites to their sulfates.[12a] This oxidation could be simply achieved by $NaIO_4$ using $RuCl_3$ as catalyst. The cyclic sulfates are then easily ring-opened by amines allowing us to form (*in situ*) their linear amino-sulfates which undergo base-assisted ring-closure to give the *N*-substituted aziridines **30**–**32** in appreciable yields. These Wecker-type cyclizations are in general accompanied by side-product formation, and typically the amino alcohol product (Scheme 2, *top*) is found in the crude reaction mixtures.[21]

Aziridines **30** and **31** are known compounds for which, however, do not exist many preparative meth-



Scheme 2. Synthesis of *N*-substituted aziridines **30**–**32** from cyclic sulfites through an oxidation, aminolysis and ring-closure sequence.

ods.[12a,22] More importantly, aziridine **32** has not been reported before and shows that the present modular protocol thus offers new potential towards a wider range of *N*-substituted aziridines including the use of poorly nucleophilic aromatic amines.

Conclusions

We here report on a new catalytic procedure for the formation of functional cyclic sulfites from a wide range of terminal and internal epoxides and SO_2 under productive Al(III) catalysis. The process is characterized by its operational simplicity, unprecedented product scope and mild reaction conditions. Furthermore, the synthetic potential of these cyclic sulfites was further demonstrated by application in *N*-substituted aziridine synthesis. The present work thus further expands the use of small molecules such as SO_2 in preparative chemistry, and offers new potential towards the construction of valuable chemicals.[23]

Experimental Section

Cyclic Sulfite Synthesis

Copper powder (9.0 mmol) was added to sulfuric acid (10 mL) and then heated to 90 °C. This reaction vessel was connected to another through a Teflon tube and an overpressure "trap" containing a solution of NaOH (2 M). The main reactor was charged with a solution of the epoxide (3.0 mmol), complex **C** (0.5–1.0 mol%) and NBu_4I (2.5–5.0 mol%) in acetonitrile (1.0 mL), and a gentle flow of N_2 was adjusted such that the *ex situ* formed SO_2 was transported towards the reactor containing the substrate/catalyst. Once the SO_2 started to form (bubbles), the reaction flask was heated to 50 °C and the mixture stirred for 3 h (terminal epoxides) or 16 h (internal epoxides). Thereafter, the solvent was removed and the product purified by column chromatography. The corresponding analytical data and NMR/IR spectra for **1**–**29** are reported in the Supporting Information.

Cyclic Sulfate Synthesis

The respective cyclic sulfite (1.0 mmol) was dissolved into acetonitrile (1.0 mL) and cooled down to 0 °C. Then $NaIO_4$ (1.2 equiv), $RuCl_3$ (1.0 mol%) and pre-cooled water (1.0 mL) were added to the reaction mixture. The mixture was stirred at room temperature for 15 min. Then the product was extracted with ethyl acetate and dried over anhydrous sodium sulfate. The crude product thus obtained was purified by column chromatography.

Aziridine Synthesis

The respective cyclic sulfate (1.0 mmol) was combined with the corresponding amine (1.2 mmol) and this mixture was stirred for 15 min, whereafter toluene (2.0 mL) and NaOH (6 M, 2.0 mL) were added. This biphasic mixture was heated to 70 °C and stirred for 12 h after which the product was extracted by ethyl acetate, concentrated and purified by column chromatography. The corresponding analytical data and NMR/IR spectra for **30**–**32** are reported in the Supporting Information.

Crystallographic Studies

The measured crystal was stable under atmospheric conditions; nevertheless it was treated under inert conditions immersed in perfluoro-polyether as protecting oil for manipulation. Data Collection: measurements were made on a Bruker-Nonius diffractometer equipped with an APPEX II 4 K CCD area detector, a FR591 rotating anode with Mo Kα radiation, Montel mirrors and a Kryoflex low temperature device ($T = -173$ °C). Full-sphere data collection was used with ω and φ scans. Programs used: data collection Apex2 V2011.3 (Bruker-Nonius 2008), data reduction Saint+Version 7.60 A (Bruker AXS 2008) and absorption correction SADABS V. 2008–1 (2008). Structure solution: SHELXTL Version 6.10 (Sheldrick, 2000) was used.[24] Structure refinement: SHELXTL-97-UNIX VERSION.

*Crystal data for cyclic sulfite **13***: $C_{14}H_{12}SO_3$, $M_r = 260.30$, monoclinic, $P2(1)$, $a = 5.7150(4)$ Å, $b = 39.165(4)$ Å, $c = 5.8138(4)$ Å, $\alpha = 90°$, $\beta = 114.065(9)°$, $\gamma = 90°$, $V = 1188.20(19)$ Å^3, $Z = 4$, $\rho = 1.455$ mg M^{-3}, $\mu = 0.269$ mm^{-1}, $\lambda = 0.71073$ Å, $T = 100(2)$ K, $F(000) = 544$, crystal size = 0.20 × 0.08 × 0.01 mm, θ(min) = 3.12°, θ(max) = 26.69°, 12372 reflections collected, 4368 reflections unique ($R_{int} = 0.0682$), GoF = 1.039, $R_1 = 0.0734$ and $wR_2 = 0.1811$ [$I > 2\sigma(I)$], $R_1 = 0.0876$ and $wR_2 = 0.1892$ (all indices), min/max residual density = −0.605/1.116 [e·Å^{-3}]. Completeness to $\theta(26.69°) = 91.0\%$.

*Crystal data for cyclic sulfite **22***: $C_4H_6SO_4$, $M_r = 150.15$, monoclinic, $P21/c$, $a = 4.3700(3)$ Å, $b = 11.7211(8)$ Å, $c = 11.1311(7)$ Å, $\alpha = 90°$, $\beta = 100.0185(19)°$, $\gamma = 90°$, $V = 561.45(6)$ Å^3, $Z = 4$, $\rho = 1.776$ mg M^{-3}, $\mu = 0.507$ mm^{-1}, $\lambda = 0.71073$ Å, $T = 100(2)$ K, $F(000) = 312$, crystal size = 0.30 × 0.15 × 0.04 mm, θ(min) = 2.54°, θ(max) = 32.51°, 6736 reflections collected, 1865 reflections unique ($R_{int} = 0.0365$), GoF = 1.046, $R_1 = 0.0316$ and $wR_2 = 0.0830$ [$I > 2\sigma(I)$], $R_1 = 0.0393$ and $wR_2 = 0.0887$ (all indices), min/max residual density = −0.312/0.544 [e·Å^{-3}]. Completeness to $\theta(32.51°) = 91.5\%$.

*Crystal data for cyclic sulfite **25***: $C_{10}H_{10}SO_3$, $M_r = 210.24$, monoclinic, $P21/c$, $a = 7.4377(13)$ Å, $b = 11.56071(19)$ Å, $c = 21.1227(4)$ Å, $\alpha = 90°$, $\beta = 90.0436(16)°$, $\gamma = 90°$, $V = 1816.24(5)$ Å^3, $Z = 8$, $\rho = 1.538$ mg M^{-3}, $\mu = 0.331$ mm^{-1}, $\lambda = 0.71073$ Å, $T = 100(2)$ K, $F(000) = 880$, crystal size = 0.20 × 0.10 × 0.10 mm, θ(min) = 2.01°, θ(max) = 36.94°, 39202 reflections collected, 8857 reflections unique ($R_{int} = 0.0294$), GoF = 1.081, $R_1 = 0.0312$ and $wR_2 = 0.0900$ [$I > 2\sigma(I)$], $R_1 = 0.0358$ and $wR_2 = 0.0942$ (all indices), min/max residual density = −0.387/0.694 [e·Å^{-3}]. Completeness to $\theta(36.94°) = 96.3\%$.

CCDC 1494964 (**13**), CCDC 1494963 (**22**) and CCDC 1494965 (**25**) contain the supplementary crystallographic data for the above compounds. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

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References

[1] a) C. R. Kennedy, S. Lin, E. N. Jacobsen, *Angew. Chem.* **2016**, *128*, 12784–12814; *Angew. Chem. Int. Ed.* **2016**, *55*, 12596–12624; b) D. W. Stephan, G. Erker, *Angew. Chem.* **2015**, *127*, 6498–6541; *Angew. Chem. Int. Ed.* **2015**, *54*, 6400–6441; c) X. Liu, L. He, Y.-M. Liu, Y. Cao, *Acc. Chem. Res.* **2014**, *47*, 793–804; d) L. Que Jr, W. B. Tolman, *Nature* **2008**, *455*, 333–340; e) Q. Liu, L. Wu, R. Jackstell, M. Beller, *Nat. Commun.* **2015**, *6*, 5933.

[2] a) T. Sakakura, J.-C. Choi, H. Yasuda, *Chem. Rev.* **2007**, *107*, 2365–2387; b) M. Aresta, A. Dibenedetto, A. Angelini, *Chem. Rev.* **2014**, *114*, 1709–1742; c) R. Martín, A. W. Kleij, *ChemSusChem* **2011**, *4*, 1259–1263; d) M. Cokoja, C. Bruckmeier, B. Rieger, W. A. Herrmann, F. E. Kühn, *Angew. Chem.* **2011**, *123*, 8662–8690; *Angew. Chem. Int. Ed.* **2011**, *50*, 8510–8537; e) X.-B. Lu, D. J. Darensbourg, *Chem. Soc. Rev.* **2012**, *41*, 1462–1484.

[3] For selected examples, see: a) J. Diebler, A. Spannenberg, T. Werner, *ChemCatChem* **2016**, *8*, 2027–2030; b) C. Beattie, M. North, *ChemCatChem* **2014**, *6*, 1252–1259; c) D. J. Darensbourg, S. J. Wilson, A. D. Yeung, *Macromolecules* **2013**, *46*, 8102–8110.

[4] For selected examples, see: a) S. Chuprakov, S. W. Kwok, V. V. Fokin, *J. Am. Chem. Soc.* **2013**, *135*, 4652–4655; b) J. A. Castro-Osma, A. Earlam, A. Lara-Sánchez, A. Otero, M. North, *ChemCatChem* **2016**, *8*, 2100–2108; c) P. Wang, J. Qin, D. Yuan, Y. Wang, Y. Yao, *ChemCatChem* **2015**, *7*, 1145–1151; d) T. Baronsky, C. Beattie, R. W. Harrington, R. Irfan, M. North, J. G. Osende, C. Young, *ACS Catal.* **2013**, *3*, 790–797.

[5] a) N. Kielland, C. J. Whiteoak, A. W. Kleij, *Adv. Synth. Catal.* **2013**, *355*, 2115–2138; b) M. Peters, B. Köhler, W. Kuckshinrichs, W. Leitner, P. Markewitz, T. E. Müller, *ChemSusChem* **2011**, *4*, 1216–1240; c) C. Martín, G. Fiorani, A. W. Kleij, *ACS Catal.* **2015**, *5*, 1353–1370; d) Y. Tsuji, T. Fujihara, *Chem. Commun.* **2012**, *48*, 9956–9964; e) C. Maeda, Y. Miyazaki, T. Ema, *Catal. Sci. Technol.* **2014**, *4*, 1482–1497; f) B. Yu, L.-N. He, *ChemSusChem* **2015**, *8*, 52–62.

[6] For an overview of its progress, see: a) E. J. Emmett, M. C. Willis, *Asian J. Org. Chem.* **2015**, *4*, 602–611; b) J. Lugiņina, *Synlett* **2014**, *25*, 2962.

[7] a) H. R. Kricheldorf, O. Petermann, *Macromolecules* **2001**, *34*, 8841–8846; b) L. S. Jeong, V. E. Marquez, *Tetrahedron Lett.* **1996**, *37*, 2353–2356; c) N. Quan, L. Nie, X. Shi, R. Zhu, X. Lü, *Chin. J. Chem.* **2012**, *30*, 2759–2766; d) A. Megia-Fernandez, J. Morales-Sanfrutos, F. Hernandez-Mateo, F. Santoyo-Gonzalez, *Curr. Org. Chem.* **2010**, *14*, 401–432. For an early review, see: e) B. B. Lohray, *Synthesis* **1992**, 1035–1052.

[8] For a few selected examples following the thionyl chloride route, see: a) A. Garcia-Granados, A. Parra, F. Rivas, A. J. Segovia, *J. Org. Chem.* **2007**, *72*, 643–646; b) S. Tanaka, Y. Sugihara, A. Sakamoto, A. Ishii, J. Nakayama, *Heteroat. Chem.* **2003**, *14*, 587–595; c) C. Hardacre, I. Messina, M. E. Migaud, K. A. Ness, S. E. Norman, *Tetrahedron* **2009**, *65*, 6341–6347; d) Y. Gao, K. B. Sharpless, *J. Am. Chem. Soc.* **1988**, *110*, 7538–7539.

[9] Cyclic sulfite synthesis from epoxides and SO_2 using various catalyst systems, see: a) Z.-Z. Yang, L.-N. He, Q.-W. Song, K.-H. Chen, A.-H. Liu, X.-M. Liu, *Phys. Chem. Chem. Phys.* **2012**, *14*, 15832–15839; b) Y. Takenaka, T. Kiyosu, G. Mori, J.-C. Choi, N. Fukaya, T. Sakakura, H. Yasuda, *ChemSusChem* **2012**, *5*, 194–199; c) Z. Florjańczyk, D. Raducha, A. Kozera-Szałkowska, *Macromolecules* **1996**, *29*, 826–834; d) Z. Florjańczyk, D. Raducha, *Makromol. Chem. Rapid Commun.* **1993**, *14*, 207–211; e) Z. Florjańczyk, A. Kozera-Szałkowska, J. Noniewicz, *Macromol. Chem. Phys.* **2002**, *203*, 565–572; f) G. A. Razuvaev, V. S. Etlis, L. N. Grobov, *J. Gen. Chem. USSR* **1961**, *31*, 1230–1233; g) Z.-Z. Yang, L.-N. He, Y.-N. Zhao, B. Yu, *Environ. Sci. Technol.* **2013**, *47*, 1598–1605; h) Y. Takenaka, J.-C. Choi, T. Sakakura, H. Yasuda, T. Kiyosu, Japanese Patent 2010037322, **2010**.

[10] a) C. J. Whiteoak, N. Kielland, V. Laserna, E. C. Escudero-Adán, E. Martin, A. W. Kleij, *J. Am. Chem. Soc.* **2013**, *135*, 1228–1231; b) C. J. Whiteoak, E. Martin, M. Martínez Belmonte, J. Benet-Buchholz, A. W. Kleij, *Adv. Synth. Catal.* **2012**, *354*, 469–476; c) C. J. Whiteoak, E. Martin, E. C. Escudero-Adán, A. W. Kleij, *Adv. Synth. Catal.* **2013**, *355*, 2233–2239; d) J. Rintjema, R. Epping, G. Fiorani, E. Martín, E. C. Escudero-Adán, A. W. Kleij, *Angew. Chem.* **2016**, *128*, 4040–4044; *Angew. Chem. Int. Ed.* **2016**, *55*, 3972–3976; e) V. Laserna, G. Fiorani, C. J. Whiteoak, E. Martin, E. Escudero-Adán, A. W. Kleij, *Angew. Chem.* **2014**, *126*, 10584–10587; *Angew. Chem. Int. Ed.* **2014**, *53*, 10416–10419; f) V. Laserna, W. Guo, A. W. Kleij, *Adv. Synth. Catal.* **2015**, *357*, 2849–2854; g) J. Rintjema, W. Guo, E. Martin, E. C. Escudero-Adán, A. W. Kleij, *Chem. Eur. J.* **2015**, *21*, 10754–10762.

[11] a) L. Peña Carrodeguas, J. González-Fabra, F. Castro-Gómez, C. Bo, A. W. Kleij, *Chem. Eur. J.* **2015**, *21*, 6115–6122; b) W. Guo, V. Laserna, E. Martin, E. C. Escudero-Adán, A. W. Kleij, *Chem. Eur. J.* **2016**, *22*, 1722–1727.

[12] a) B. B. Lohray, Y. Gao, K. B. Sharpless, *Tetrahedron Lett.* **1989**, *30*, 2623–2626; b) C. Xiong, W. Wang, V. J. Hruby, *J. Org. Chem.* **2002**, *67*, 3514–3517; c) B. R. Buckley, A. P. Patel, K. G. U. Wijayantha, *J. Org. Chem.* **2013**, *78*, 1289–1292; d) X. Li, N. Chen, J. Xu, *Synthesis* **2010**, 3423–3428.

[13] For some examples of recent use of DABSO in organic synthesis, see: a) A. S. Deeming, C. J. Russell, M. C. Willis, *Angew. Chem.* **2016**, *128*, 757–760; *Angew. Chem. Int. Ed.* **2016**, *55*, 747–750; b) B. N. Rocke, K. B. Bahnck, M. Herr, S. Lavergne, V. Mascitti, C. Per-

reault, J. Polivkova, A. Shavnya, *Org. Lett.* **2014**, *16*, 154–157.

[14] Ammonium halides alone are known to be moderately good mediators of cyclic sulphite formation, refer, for instance, to refs.[9a,b]

[15] See, for instance: a) C. J. Whiteoak, B. Gjoka, E. Martin, M. Martínez Belmonte, E. C. Escudero-Adán, C. Zonta, G. Licini, A. W. Kleij, *Inorg. Chem.* **2012**, *51*, 10639–10649; b) J. W. Hwang, K. Govindaswamy, S. A. Koch, *Chem. Commun.* **1998**, 1667–1668; c) W. Su, Y. Kim, A. Ellern, I. A. Guzei, J. G. J. Verkade, *J. Am. Chem. Soc.* **2006**, *128*, 13727–13735.

[16] We checked the *dr* before (88:12) and after crystallization (96:4) and noted that it had further increased. This suggests that the major isomer had crystallized.

[17] Since we used a gentle nitrogen flow to transport the *ex situ* SO_2 to the actual reactor, in those cases where volatile epoxides were used the yield was slightly compromised by loss of substrate through evaporation.

[18] The Al-catalyzed Meinwald rearrangement has been reported, see: a) J. R. Lamb, Y. Jung, G. W. Coates, *Org. Chem. Front.* **2015**, *2*, 346–349; b) J. R. Lamb, M. Mulzer, A. M. LaPointe, G. W. Coates, *J. Am. Chem. Soc.* **2015**, *137*, 15049–15054.

[19] Such back-biting processes that control the stereochemistry of the cyclic sulfite carbonate formation have been known, see: a) K. Soga, I. Hattori, J. Kinoshita, S. Ikeda, *J. Polym. Sci. Pol. Chem.* **1977**, *15*, 745-753. See also refs.[9c,d] Note that only in the synthesis of **19** we were able detect a polymeric intermediate. However, the presence of both *cis* and *trans* configured products noted for compounds **20**, **24**, **25**, **28** and **29** seems to suggest that some degree of *in situ* oligomerization takes place following back-biting of the oligomeric intermediates leading to the *trans* cyclic sulfites. It is also likely that such oligomer formation takes place at the Al metal complex (and not in the absence of it) as recent work from Jia et al. demonstrated that in the absence of a catalyst only cyclic product was formed, see: b) Y. Zhi, J. Wu, A. Ma, N. Tian, S. Shan, Q. Jia, H. Su, *RSC Adv.* **2016**, *6*, 32881–32886. Furthermore, the excess nucleophile used (2.5–5.0 equiv. *versus* Al catalyst) should also favour cyclic over poly-sulfite formation, and if formed, polymer degradation.

[20] The formation of *trans*-**24** from *cis*-2,3-epoxybutane could be the result of *in situ* oligo/poly-sulfite formation following degradation that would lead then to a *trans* configuration in the cyclic sulfite product. The same epoxide has been shown by Darensbourg to react with CO_2 to mixtures of poly- and cyclic carbonates: for the latter also some loss of stereo-retention was noted. See: D. J. Darensbourg, W.-C. Chung, *Macromolecules* **2014**, *47*, 4943–4948.

[21] Wecker-type cyclizations yielding aziridine products in similar yields as reported for **30–32** with amino alcohol by-product formation has been well documented, see refs.[12c,d]

[22] As far as we are aware, only few reports exist for the formation of **30** and **31**, see: a) D. Kühnau, I. Thomsen, K. A. Jörgensen, *J. Chem. Soc. Perkin Trans. 1* **1996**, 1167–1170; b) S. Sternativo, F. Marini, F. Del Verme, A. Calandriello, L. Testaferri, M. Tiecco, *Tetrahedron* **2010**, *66*, 6851–6857; c) K. J. Shaw, J. R. Luly, H. Rapoport, *J. Org. Chem.* **1985**, *50*, 4515–4523.

[23] For highly recent uses of cyclic sulfates in cross-coupling chemistry, see: a) R. Ramírez-Contreras, B. Morandi, *Org. Lett.* **2016**, *18*, 3718–3723; b) M. S. Eno, A. Lu, J. P. Morken, *J. Am. Chem. Soc.* **2016**, *138*, 7824–7827.

[24] G. M. Sheldrick, *SHELXTL Crystallographic System*, version 6.10; Bruker AXS, Inc.: Madison, WI, **2000**.

Aluminum-Catalyzed Formation of Functional 1,3,2-Dioxathiolane 2-Oxides from Sulfur Dioxide: An Easy Entry towards *N*-Substituted Aziridines

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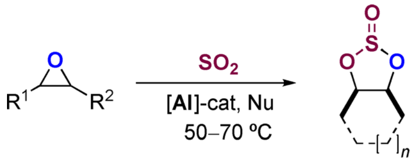

- mild conditions
- chemoselective, good yields
- 29 examples, yield up to 95%
- precursors for aziridines