Aluminum Catalyzed formation of Functional 1,3,2-Dioxathiolane 2-Oxides from SO_2: An Easy Entry towards N-Substituted Aziridines

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Abstract. Al(III) complexes derived from aminotriphenolate ligands are shown to be excellent catalysts for the formation of cyclic sulphites from a range of (functionalized) terminal and internal epoxides, and *ex situ* generated sulphur 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 (50–70ºC, $p(SO_2) < 1$ bar). The synthetic potential of these cyclic sulphites in organic synthesis is demonstrated in the preparation of *N*-substituted aziridines through a three-step protocol.

**Keywords:** Aluminum; Aziridines; Cyclic Sulphites; Homogeneous Catalysis; Sulphur 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 disulphide (CS_2)[3] and isocyanates (R−NCO)[4] has received a great deal of attention enabling the synthesis of various heterocyclic structures. Whereas the use of CO_2 as a carbon synthon in synthesis has now been well-established,[5] the use of sulphur 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 sulphites (*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 sulphites. In particular, low-temperature conversions and further widening the scope in reaction partners may be required to valorise these cyclic sulphites as chemical building blocks. To this end, isolation of the pure sulphite targets is often hampered due to the presence of mixture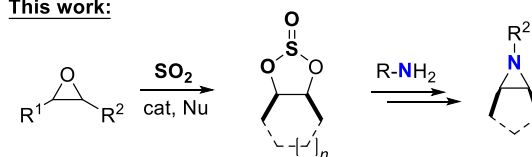s of poly- and cyclic sulphites. Moreover, as far as we know only limited potential towards the more challenging coupling of internal epoxides and SO_2 has been reported to date. Consequently, this restricts the synthesis of cyclic sulphites mostly to the use of terminal oxiranes.
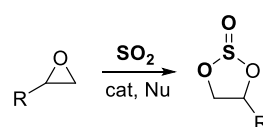
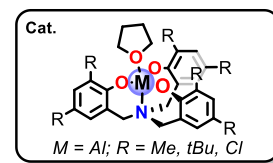**Scheme 1**. Conversion of SO_2 into cyclic sulphites by reaction with epoxides: below the current approach.

In recent years, we have reported on the application of highly reactive and versatile Al(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 sulphites, 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 sulphur-containing heterocycles in good to excellent isolated yields under attractive mild conditions. Furthermore, the use of these cyclic sulphites as molecular synthons is demonstrated in the preparation of *N*-substituted aziridines, which can be easily obtained through oxidation of the sulphite to a sulphate intermediate followed by subsequent aminolysis and a Wenker type base-assisted cyclization.[12]

Results and Discussion

Our first attempts to produce cyclic sulphites 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 (NBu₄I) 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 than 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 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 sulphite **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 (Supporting Information for more details) to transport the reactant to a reactor containing the epoxide and catalyst should deliver a more productive protocol for cyclic sulphite 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.

Table 1. Screening study towards the formation of the cyclic sulphite product **1** derived from 1,2-epoxyhexane and DABSO using various catalysts and solvents.[a]
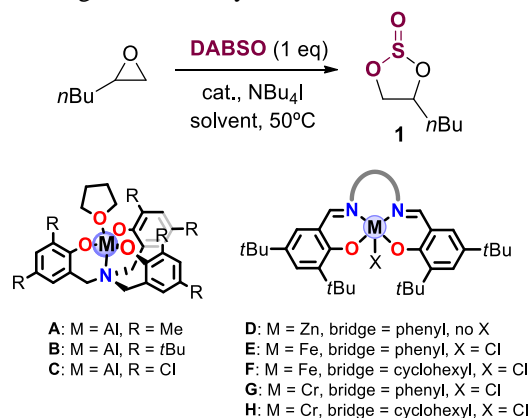
Entry	Cat.	Solvent	t [h]	Yield [%][b]
1	**A**	CH₃CN	3	41
2	**B**	CH₃CN	3	51
3	**C**	CH₃CN	3	55 (63)[c]
4	**D**	CH₃CN	3	45 (49)[c]
5	**E**	CH₃CN	3	31
6	**F**	CH₃CN	3	26
7	**G**	CH₃CN	3	30
8	**H**	CH₃CN	3	47 (58)[c]
9	**C**	EtOAc	6	59
10	**C**	THF	6	23
11	**C**	DMF	6	24
12	**C**	MEK	6	19
13	**–**	CH₃CN	3	45

[a] General conditions: 3.0 mmol of 1,2-epoxyhexane, 2.5 mol% cat., 5.0 mol% NBu₄I, solvent indicated (1 mL), 50ºC, 1 eq DABSO. [b] Isolated yield. [c] Isolated yield after a 6 h reaction time.

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 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 (70ºC, entry 11) did not
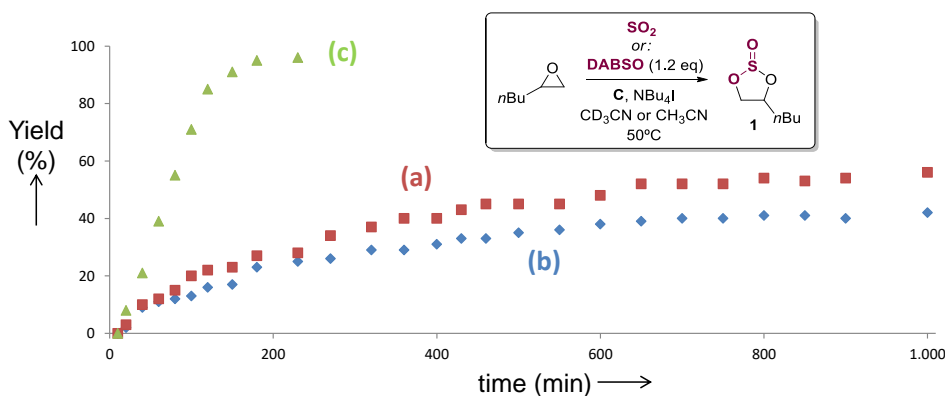
Figure 1. Kinetic profiles determined by ^{1}H NMR (CD$_3$CN) for the synthesis of **1** using DABSO (1.2 eq.) and mesitylene as internal standard. (a) Using **C**/NBu$_4$I as binarycatalyst; (b) Only NBu$_4$I; (c) Reaction performed with *ex-situ* generated SO$_2$ from H$_2$SO$_4$/Cu: epoxide (3 mmol), C (1.0 mol%), NBu$_4$I (2.5 mol%), CH$_3$CN (1.0 mL), 50ºC.

Table 2. Optimization of the protocol involving *ex situ* SO$_2$ formation from Cu/H$_2$SO$_4$ using catalysts **A–C**/NBu$_4$X and CH$_3$CN in the formation of the cyclic sulphite product **1**.[a]

Entry	Cat. [mol%]	Nu [mol%]	T [ºC]	Yield [%][b]
1	–	NBu$_4$I (1.0)	50	11
2	–	NBu$_4$I (2.5)	50	29
3	–	NBu$_4$I (5.0)	50	61
4	–	NBu$_4$Br (2.5)	50	25
5	**C** (0.5)	NBu$_4$I (2.5)	50	85
6	**B** (0.5)	NBu$_4$I (2.5)	50	41
7	**A** (0.5)	NBu$_4$I (2.5)	50	65
8	**C** (1.0)	NBu$_4$I (2.5)	50	86
9	**C** (1.0)	NBu$_4$I (1.0)	50	61
10	**C** (0.5)	NBu$_4$I (2.5)	25	22
11	**C** (0.5)	NBu$_4$I (2.5)	70	84

[a] General conditions: 3.0 mmol of 1,2-epoxyhexane, **C** (amount indicated), NBu$_4$X (amount indicated), CH$_3$CN (1 mL), Cu (3 eq.) in H$_2$SO$_4$ (10 mL) at 90ºC (*ex situ*), 2 h. [b] NMR yields based on mesitylene as an internal standard.

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 sulphites (*cf.*, formation of compounds **1–18**, Figure 2) using 1.0 mol% of Al-complex **C**, 2.5 mol% of NBu$_4$I in CH$_3$CN at 50ºC. Under these conditions, cyclic sulphite **1** could be isolated in excellent yield (93%) as a mixture of two diastereoisomers in a 82:18 ratio. The presence of two diastereo-isomers is the result of the non-planarity of the cyclic sulphite, with the sulphur lone pair either being on the same or opposite side of the ring substituent. The two diastereo-isomers are well-separated and assignable by NMR analysis (see Supporting Information). For instance, for **1** the major isomer is characterized by three distinct signals for the hydrogens attached to the sulphite ring whereas the minor isomer shows only
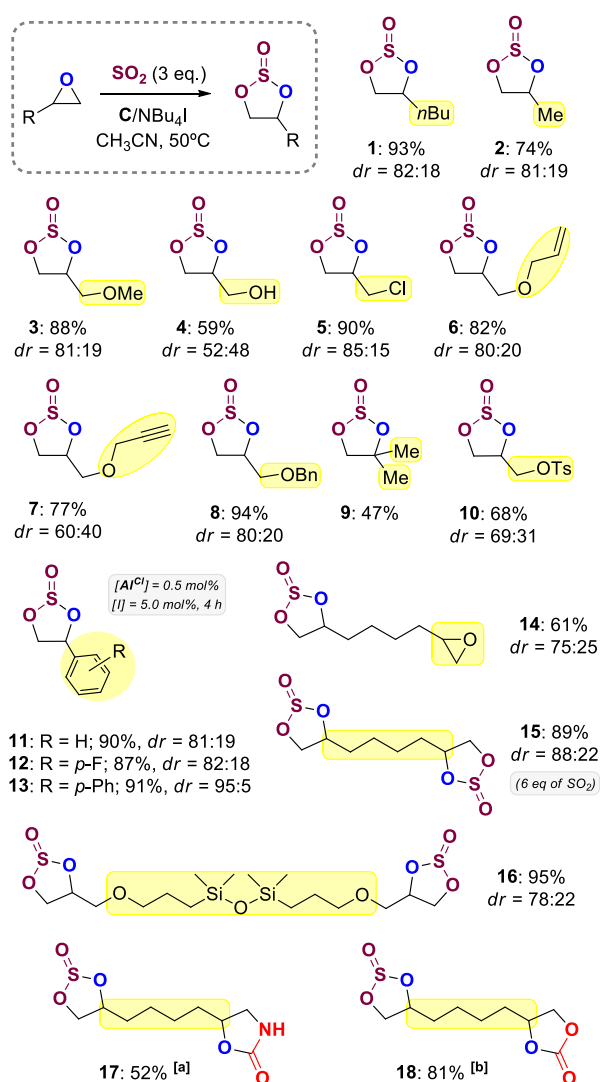

Figure 2. Synthesis of cyclic sulphites **1–18** from various terminal epoxides using *ex situ* generated SO$_2$. Conditions (unless stated otherwise): complex **C** (1.0 mol%), NBu$_4$I (2.5 mol%), CH$_3$CN (1.0 mL), 50ºC, 3 h. Reported yields are isolated ones after column purification. [a] From cyclic sulphite **14**; 1.2 eq of phenyl carbamate, 5.0 mol% C, 18 h, 50ºC, CH$_3$CN. [b] 0.5 mol% **C**, 2.5 mol % NBu$_4$I, 10 bar CO$_2$, 6 h, 50ºC, MEK. *Dr*'s were determined by ^{1}H NMR.

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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 seem to suggest that this diastereo-isomer has the sulphur 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 sulphite **13** could be determined (Figure 3): the relative orientation of the ring-substituent (*p*-biphenylene) and the sulphur lone pair is in line with the NMR observations for **1** and most of the other isolated products.[16]
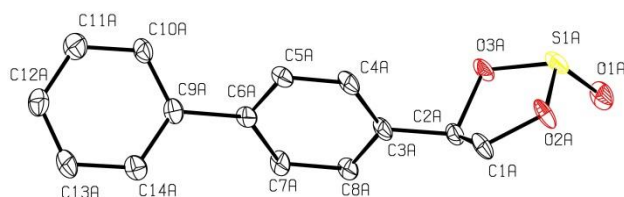

Figure 3. X-ray molecular structure for **13**. Selected bond lengths (Å) and angles (º): S(1A)-O(1) = 1.454(7), S(1A)-O(2A) = 1.633(6), S(1A)-O(3A) = 1.614(6); O(1A)-S(1A)-O(2A) = 105.3(4), O(1A)-S(1A)-O(3A) = 108.9(4).

Many different and potentially useful substituents onto the cyclic sulphite 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 centre in **C**.[17] In those cases where styrene oxides were used (*cf.*, the formation of **11–13**), a higher loading of the nucleophile was required as to prevent significant formation of ketone by-products through Meinwald rearrangement.[18] Interestingly, mono-sulphite **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 eq., the bis-sulphite **15** was obtained as the major compound and isolated in good yield (89%). Compound **14** could be easily converted into the mixed sulphite/carbamate **17** (52%) and sulphite/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 sulphites.

Motivated by the successful preparation of functional mono-substituted sulphites, 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** (50ºC, 3 eq. of SO_2, 1.0 mol% of **C**). However, NBu4Br 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 50ºC proved to be a bit sluggish and, moreover, ^{1}H NMR analysis showed the presence of peaks reminiscent of poly-sulphites with only trace amounts of cyclic product. Therefore, the reaction between CHO and SO_2 mediated by complex **C**/NBu4Br was then carried out at 70ºC using longer reaction times, and to our delight we found that the reaction mixture contained virtually only the cyclic sulphite product **19** (Supporting Information for more details). The latter was isolated in moderate yield (46%; Figure 4) by chromatographic purification.
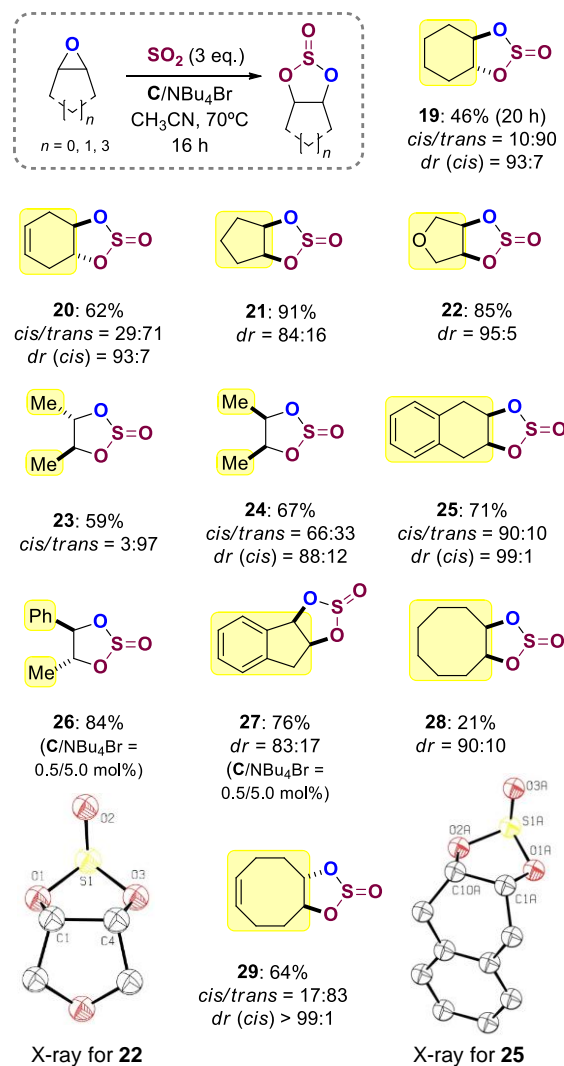

Figure 4. Synthesis of cyclic sulphites **19–29** from internal epoxides using *ex situ* generated SO_2. Conditions (unless stated otherwise): complex **C** (1.0 mol%), NBu4Br (2.5 mol%), CH_3CN (1.0 mL), 70ºC, 16 h. Reported yields are isolated ones after column purification. *Cis/trans* assignments and *dr* ratios were determined by ^{1}H NMR. Note that for the *cis/trans* mixtures, only the major isomer is drawn in the Figure.

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Notably, compound **19** was mostly isolated as the *trans* isomer which is the expected result if the cyclic sulphite would be formed by back-biting of an initially formed poly-sulphite polymer.[19]

Then other internal epoxides were examined as reaction partners thereby producing the cyclic sulphites **20–29** generally in appreciable yields (except for **28**; 21%). The more rigid nature of the 8-membered ring epoxide leading to cyclic sulphite **29** delivers the product in much better yield (64%) than noted for **28**: such 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) centre in complex **C** thereby complicating nucleophile-assisted ring-opening. The introduction of a double bond in the 8-membered ring reduces the conformational complexity and flexibility, and this should facilitate better its conversion into the cyclic sulphite. 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 sulphides from SO_2. For the conversion of *trans*-2,3-dimethyloxirane (leading to **23**) and its *cis*-isomer (giving rise to **24**) 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]
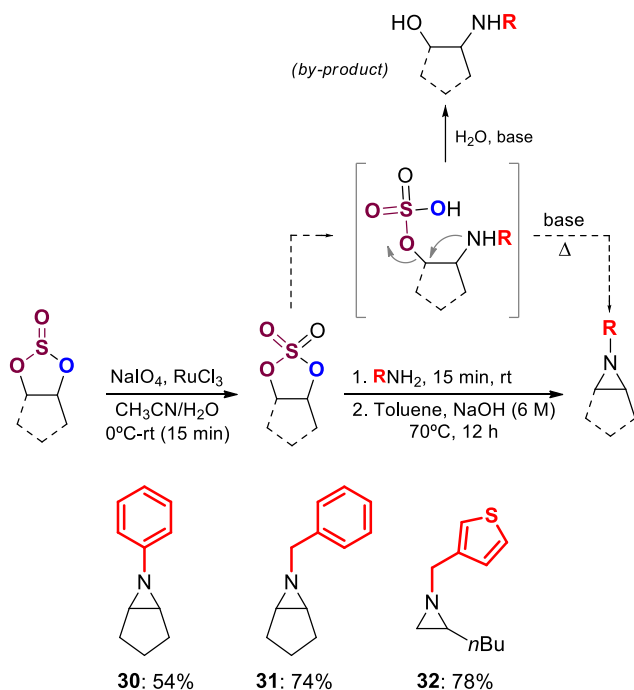
All new compounds were completely characterized by IR/NMR spectroscopic techniques, and high-resolution mass analyses. In addition, the structures of **22** and **25** were also confirmed by X-ray analyses (Figure 4, below). In the determined molecular structures, the same mutual orientation of the sulphur lone pair and the cyclic sulphide ring substituents was found as revealed for **13** (Figure 3).

In order to investigate further the potential of these cyclic sulphites in organic synthesis, we considered the formation of aziridines by first oxidizing the respective sulphites to their sulphates.[12a] This oxidation could be simply achieved by $NaIO_4$ using $RuCl_3$ as catalyst. The cyclic sulphates are then easily ring-opened by amines allowing to form (*in situ*) their linear amino-sulphates 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 by-product formation, and typically the amino-alcohol product (Scheme 2, top) is found in the crude reaction mixtures.[21]

Azirines **30** and **31** are known compounds for which, however, do not exist many preparative methods.[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.

Conclusion

We here report on a new catalytic procedure for the formation of functional cyclic sulphites 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 sulphites 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 Sulphite Synthesis

Copper powder (9.0 mmol) was added to sulphuric acid (10 mL) and then heated to 90ºC. 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 50ºC and the mixture stirred for 3 h (terminal epoxides) or 16 h (internal epoxides). Hereafter, the solvent was removed and the product purified by column chromatography. The corresponding analytical data and

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

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NMR/IR spectra for **1–29** are reported in the Supporting Information.

Cyclic Sulphate Synthesis

The respective cyclic sulphite (1.0 mmol) was dissolved into acetonitrile (1.0 mL) and cooled down to 0ºC. Then $NaIO_4$ (1.2 eq), $RuCl_3$ (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 on anhydrous sodium sulphate. The crude product thus obtained was purified by column chromatography.

Aziridine Synthesis

The respective cyclic sulphate (1.0 mmol) was combined with the corresponding amine (1.2 mmol) and this mixture was stirred for 15 min, where after toluene (2.0 mL) and NaOH (6 M, 2.0 mL) were added. This biphasic mixture was heated to 70ºC 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 4K 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 7.60A (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 sulphite **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, α = 90º, β = 114.065(9)º, γ = 90º, V = 1188.20(19) Å^3, Z = 4, ρ = 1.455 mg·M^{-3}, μ = 0.269 mm^{-1}, λ = 0.71073 Å, T = 100(2) K, $F(000)$ = 544, crystal size = 0.20 × 0.08 × 0.01 mm, θ(min) = 3.12º, θ(max) = 26.69º, 12372 reflections collected, 4368 reflections unique (R_{int} = 0.0682), GoF = 1.039, R_1 = 0.0734 and wR_2 = 0.1811 [I > 2σ(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 θ(26.69°) = 91.0%. CCDC number 1494964.

Crystal data for cyclic sulphite **22**: $C_4H_6SO_4$, M_r = 150,15, monoclinic, $P2(1)/c$, a = 4.3700(3) Å, b = 11.7211(8) Å, c = 11.1311(7) Å, α = 90º, β = 100.0185(19)º, γ = 90º, V = 561.45(6) Å^3, Z = 4, ρ = 1.776 mg·M^{-3}, μ = 0.507 mm^{-1}, λ = 0.71073 Å, T = 100(2) K, $F(000)$ = 312, crystal size = 0.30 × 0.15 × 0.04 mm, θ(min) = 2.54º, θ(max) = 32.51º, 6736 reflections collected, 1865 reflections unique (R_{int} = 0.0365), GoF = 1.046, R_1 = 0.0316 and wR_2 = 0.0830 [I > 2σ(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 θ(32.51°) = 91.5%. CCDC number 1494963.

Crystal data for cyclic sulphite **25**: $C_{10}H_{10}SO_3$, M_r = 210.24, monoclinic, $P2(1)/c$, a = 7.4377(13) Å, b = 11.56071(19) Å, c = 21.1227(4) Å, α = 90º, β = 90.0436(16)º, γ = 90º, V = 1816.24(5) Å^3, Z = 8, ρ = 1.538 mg·M^{-3}, μ = 0.331 mm^{-1}, λ = 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 > 2σ(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 θ(36.94°) = 96.3%. CCDC number 1494965.

References

[1] a) C. R. Kennedy, S. Lin, E. N. Jacobsen *Angew. Chem. Int. Ed.* **2016**, DOI: 10.1002/anie.201600547; b) D. W. Stephan, G. Erker, *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. 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: 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; e) B. Yu, L.-N. He, *ChemSusChem* **2015**, *8*, 52-62.

[6] For an overview of its progress: a) E. J. Emmett, M. C. Willis, *Asian J. Org. Chem*. **2015**, *4*, 602-611; b) J. Luginiņa, *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: 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, *Heteroatom 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 sulphite synthesis from epoxides and SO_2 using various catalyst systems: 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, JP 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. Int. Ed.* **2016**, *55*, 3972-3976; e) V. Laserna, G. Fiorani, C. J. Whiteoak, E. Martin, E. Escudero-Adán, A. W. Kleij, *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: a) A. S. Deeming, C. J. Russell, M. C. Willis, *Angew. Chem. Int. Ed.* **2016**, *55*, 747-750; b) B. N.

Rocke, K. B. Bahnck, M. Herr, S. Lavergne, V. Mascitti, C. Perreault, 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 references 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] 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 stereo-chemistry of the cyclic sulphite carbonate formation have been known: a) K. Soga, I. Hattori, J. Kinoshita, S. Ikeda, *J. Polym. Sci. Pol. Chem.* **1977**, *15*, 745- 753. See also references 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 some degree of *in situ* oligomerization takes place following back-biting of the oligomeric intermediates leading to the *trans* cyclic sulphites. 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 favor cyclic over poly-sulphite 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-sulphide formation following degradation that would lead then to a *trans* configuration in the cyclic sulphide 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 references 12c and 12d.

[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. I* **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**, DOI: 10.1021/acs.orglett.6b01745; 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 Highly Functional 1,3,2-Dioxathiolane 2-Oxides from SO2: An Easy Entry towards *N*-Substituted Aziridines

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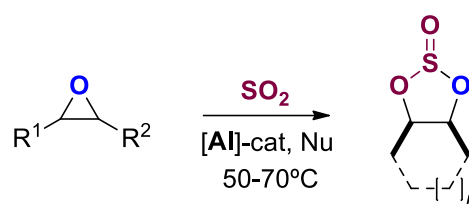
- mild conditions
- chemo-selective, good yields
- 29 examples, yield up to 95%
- precursors for aziridines