

Chapter 2

Sulfur Dioxide Surrogates

Abstract The most significant driving force in the field of sulfur dioxide insertion has been the development of safe and bench-stable sulfur dioxide surrogates. To date, several sulfur dioxide surrogates have been developed and proved to be efficient in the processes of sulfur dioxide insertion. Among them, DABCO·(SO₂)₂ (named DABSO) and potassium metabisulfite (K₂S₂O₅) are two of the most commonly used sulfur dioxide surrogates, which have been identified and documented in various transformations. In this chapter, we will introduce these sulfur dioxide surrogates, with an emphasis on those utilized in sulfur dioxide insertion reactions.

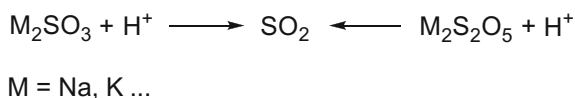
Keywords Sulfur dioxide surrogates • Potassium metabisulfite • DABCO·(SO₂)₂ • Rongalite

Utilization of surrogates for sulfur dioxide is a practical and convenient method because it avoids the need of specialized pressure-resistant equipment and reduces the safety risks due to the toxic and gaseous properties of sulfur dioxide [1–4]. As the conditions with large excess of sulfur dioxide would cause catalyst sequestration in metal-catalyzed reactions, the loading of sulfur dioxide is also necessary to be controllable. Thus, the most significant driving force in the field of sulfur dioxide insertion has been the development of safe and bench-stable sulfur dioxide surrogates. Several sulfur dioxide surrogates, including metal sulfite salts, DABCO·(SO₂)₂ (named DABSO), SOCl₂ with water, and sodium formaldehyde sulfoxylate (named rongalite), have been demonstrated to be feasible in the processes of sulfur dioxide insertion (Scheme 2.1). In the meantime, there are also some other sulfur dioxide surrogates with some applications in organic synthesis and biological systems, although they have not been utilized in sulfur dioxide insertion reactions till now.

It is well established that treatment of metal sulfites/disulfites (M₂SO₃, M₂S₂O₅) with protonic acid would release sulfur dioxide gas (Scheme 2.2). These inorganic sulfites are commercially available, inexpensive and easy-to-handle, making them attractive and reliable as sulfur dioxide surrogates. Sodium sulfite (Na₂SO₃) has been used *ex situ* with the gas produced and being transferred into the sulfur



Scheme 2.1 Commonly used sulfur dioxide surrogates in sulfur dioxide insertion reactions



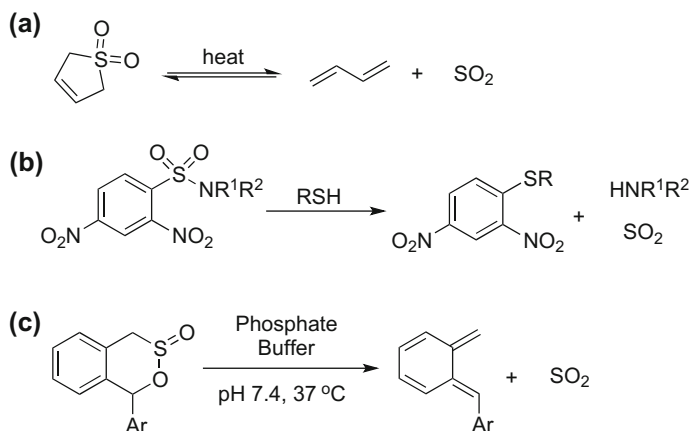
Scheme 2.2 Decomposition of metal sulfites/disulfites under acidic conditions

dioxide insertion reactions [5]. And $\text{K}_2\text{S}_2\text{O}_5$ has been particularly applied as a source of sulfur dioxide in a number of transformations, pioneered by the Wu group from Fudan University [6].

Sulfur dioxide could also be produced in situ through the reaction of thionyl chloride with water and participates in Sandmeyer sulfonyl chloride formation [7]. However, this rapid and exothermic reaction, together with the byproduct HCl, might lead to potential incompatibility. Thus, this procedure appears to be less attractive and practical, which only has a few limited applications in Sandmeyer reaction.

Rongalite (sodium formaldehyde sulfoxylate, with the chemical formula $\text{HOCH}_2\text{SO}_2\text{Na}\cdot 2\text{H}_2\text{O}$) is commercially available and cheap, and has been widely used in a variety of synthetic transformations, which also provide approaches for symmetrical dialkyl sulfones [8]. Although this reagent introduces a $-\text{SO}_2-$ unit into molecules, we have to point out that it is a source of anion radical $\text{SO}_2^{\cdot-}$ as well as anion SO_2^{2-} , rather than a source of SO_2 [9]. Inspired by the recent progress in sulfur dioxide insertion reactions, the exploration of its novel reactivity in organic synthesis has come into notice. Considering these processes also introduce a sulfonyl unit into molecules, some representative examples will also be described in detail in Chap. 3.

The amine- SO_2 adducts have been exploited over a hundred of years ago, and early relevant studies mainly focused on the investigation of their structure and bonding, rather than application as a source of sulfur dioxide [10]. In 2010, the Willis group documented the utilization of $\text{DABCO}\cdot(\text{SO}_2)_2$ (1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide), named by the authors as DABSO) as a reliable sulfur dioxide surrogate, which also represents the first utilization of a sulfur dioxide surrogate in organic chemistry [11]. This complex is a bench-stable, easy-to-handle white solid, and now represents the most commonly used sulfur dioxide surrogate.



Scheme 2.3 Other types of sulfur dioxide surrogates

General procedure for the synthesis of DABSO: A 50 mL round bottom flask was fitted with a condenser, attached to a Dreschel bottle bubbler system and flushed with argon for 10 min. 1,4-Diazabicyclo[2.2.2]octane (DABCO) (2.00 g, 16.4 mmol) was added to the flask and the system flushed with argon for a further 5 min. Sulfur dioxide gas was introduced into the system (approx. 1 bubble/sec) for 5 min. The reaction flask was cooled to $-20\text{ }^{\circ}\text{C}$ and the condenser to $-78\text{ }^{\circ}\text{C}$ and the sulfur dioxide was allowed to condense dropwisely onto the DABCO with stirring until the solid was completely covered with liquid sulfur dioxide (approx. 20 mL). The sulfur dioxide flow was stopped and the flask allowed to warm up to $-10\text{ }^{\circ}\text{C}$ and left stirring at reflux for 1 h. The condenser and bubbler were removed and the excess liquid sulfur dioxide was allowed to evaporate at room temperature under a flow of argon to reveal the complex as a white solid.

There are also some other procedures to access sulfur dioxide into necessary situations. 3-Sulfolene is another sulfur dioxide surrogate, it would release sulfur dioxide through a thermal cheletropic extrusion reaction (Scheme 2.3a) [12]. This process has been used for reduction of *N*-oxides, as well as isomerization of steroidal alkenes. Moreover, the application of sulfur dioxide surrogates including 2,4-dinitrobenzene sulfonamides [13] and 1-aryl-benzosultine derivatives [14] in biological systems has recently emerged (Scheme 2.3b, c).

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