

SYNLETT Spotlight 121

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Sulfur Dioxide

Compiled by Freddy Fonquerne

Freddy Fonquerne was born in 1978 in Briançon, France. He studied chemistry at the University Louis Pasteur of Strasbourg where he graduated from the European School of Chemistry, Polymers and Materials (ECPM) and obtained a Master's degree. Then, he moved to Lausanne (Switzerland) where he is currently in the last year of his Ph.D. studies at the Ecole Polytechnique Fédérale de Lausanne (EPFL) under the supervision of Prof. Pierre Vogel. His area of research includes the Umpolung of dienes with sulfur dioxide and applications to natural product synthesis.

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Dedicated to my father



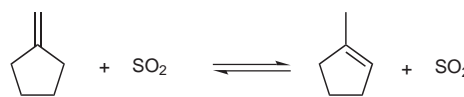
Introduction

Sulfur dioxide, obtained by burning sulfur in air, is a useful and suitable solvent and reagent for a large number of reactions.^{1,2} It has a broad liquid range (mp $-75\text{ }^{\circ}\text{C}$ and bp $-10\text{ }^{\circ}\text{C}$), a comparably high solvation power for both ionic and covalent compounds, and low nucleophilicity.

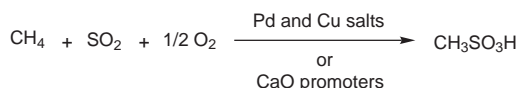
It is also a Lewis acid that is able to complex unsaturated organic compounds. Recently, this reagent has been used in the synthesis of long chain polyketides,³ sulfones, sulfinates, sulfonamides, and methanesulfonic acid.

Abstracts

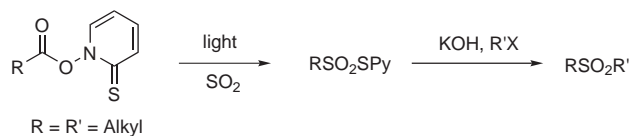
(A) Alkenes are isomerized by sulfur dioxide. The process is generally explained by invoking an ene reaction between an SO_2 molecule and the alkene.⁴ Recently, Vogel et al. revised this mechanism⁵ and showed that polysulfones resulting from the copolymerization of alkenes and SO_2 catalyze the reaction. This has led to the development of a new method for the selective cleavage of methyl-substituted allyl ethers under neutral conditions.⁶



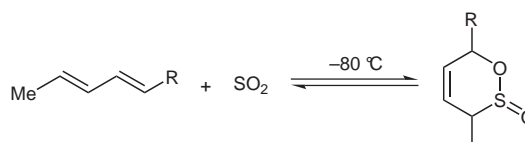
(B) Methane is transformed selectively to methanesulfonic acid at low temperature by liquid-phase sulfonation of methane with SO_2 and O_2 in the presence of Pd salts and Cu salts⁷ as the catalysts or of CaO as promoter.⁸



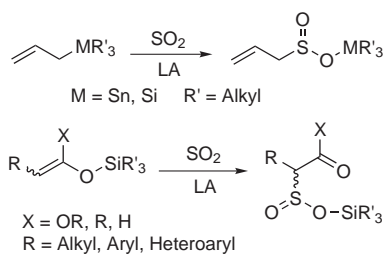
(C) Irradiation of *N*-hydroxy-2-thiopyridone esters with visible light in the presence of sulfur dioxide gives the corresponding thio-sulfonates. These can be converted into sulfones by treatment with KOH and an alkylating agent.⁹



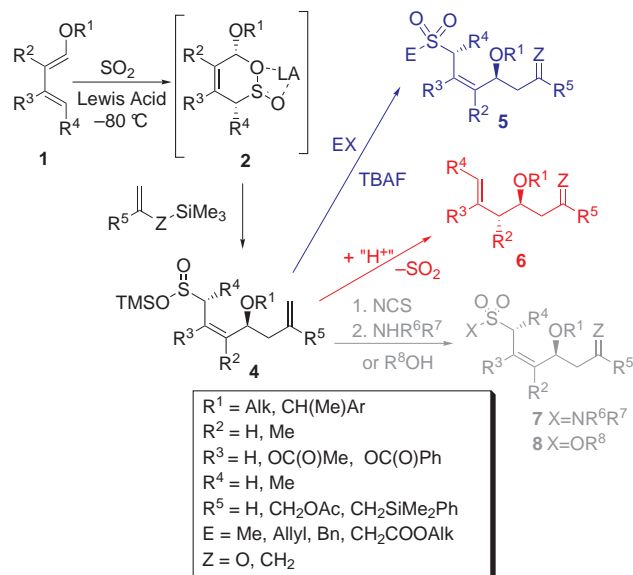
(D) 1,3-Dienes undergo hetero Diels–Alder reactions with SO_2 at low temperature in the presence of an acid promoter, such as $\text{CF}_3\text{CO}_2\text{H}$ or $\text{BF}_3 \cdot \text{Et}_2\text{O}$, leading to sultines.¹⁰



(E) Allyl tin derivatives undergo ene reactions with sulfur dioxide, furnishing tin allyl sulfonates.¹¹ Recently, it was shown that allylsilanes and enoxysilanes derived from aldehydes, ketones and esters also produce ene adducts with SO₂.¹² The silyl sulfonates from ene reactions can be brominated (Br₂ or NBS) or chlorinated (Cl₂ or NCS) to produce the corresponding sulfonyl halides. The latter react with primary or secondary amines or alcohols to give the corresponding sulfonamides or sulfonic esters (one-pot, three-component syntheses).¹³



(F) Sultines **2**, arising from HDA reactions between dienes **1** and SO₂, can be quenched with carbon nucleophiles such as enoxysilanes or allylsilanes to give silyl sulfonates **4**. Desilylation of **4** and reaction with carbon electrophiles generates polyfunctional sulfones in one-pot, four-component operations.¹⁴ Alternatively, **4** can be oxidized with NCS and reacted with amines or alcohols to produce polyfunctional sulfonamides **6** or sulfonic esters **7**, containing up to three stereogenic centers. Hydrolysis of silyl sulfonates **4** and subsequent desulfitation generates polyketides and analogs **8**, also in one-pot operations.¹⁵



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