

SYNLETT Spotlight 439

1,4-Diazabicyclo[2.2.2]octane Bis(sulfur dioxide) Adduct (DABSO)

Compiled by Ludovic Martial



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

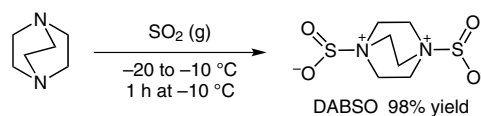
Ludovic Martial was born in France in 1986. He received his B.Sc. in molecular chemistry at the University of Aix-Marseille III, and his M.Sc. in Physics and Chemistry of Medicines at the University of Rouen. He is currently completing his Ph.D. at the University of Rouen under the guidance of Professor Laurent Bischoff. His research interest focusses on further studies of the Mitsunobu reaction: alkylation of ammonium and a semi-mineral process.

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Introduction

1,4-diazabicyclo[2.2.2]octane bis (sulfur dioxide) adduct (DABSO)¹ consists of a 1:2 complex of DABCO with sulfur dioxide. This reagent has recently found various applications, such as sulfonamide formation via palladium coupling, or synthesis of sulfonylureas. It is a colorless, stable, yet hygroscopic powder and it is more convenient to handle and safer than gaseous sulfur dioxide. In addition, the health and safety regulations concerning the transportation and storage of gaseous sulfur dioxide make DABSO even more useful. However, DABSO is an expensive commercially available reagent, generally sold only in gram-scale amounts, currently produced by few chemical suppliers. Its preparation is described in the lit-

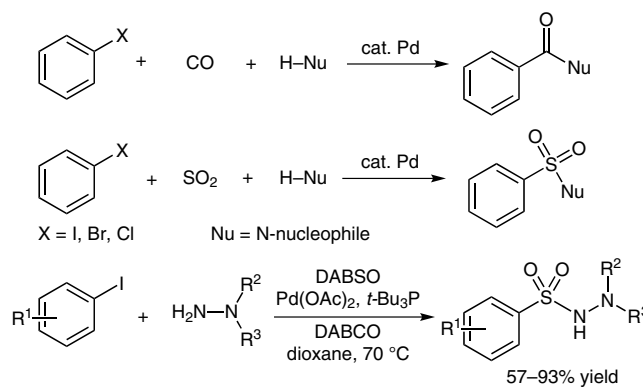
erature using gaseous sulfur dioxide which is condensed or bubbled through a solution of DABCO. This procedure uses a large excess of toxic sulfur dioxide, which should be trapped to avoid discarding in the atmosphere. As a surrogate for SO₂, DABSO can be used to form sulfonyl derivatives following two different pathways: either starting from aryl halides under palladium catalysis, or with a C- or N-nucleophile in the presence of an oxidizing agent.



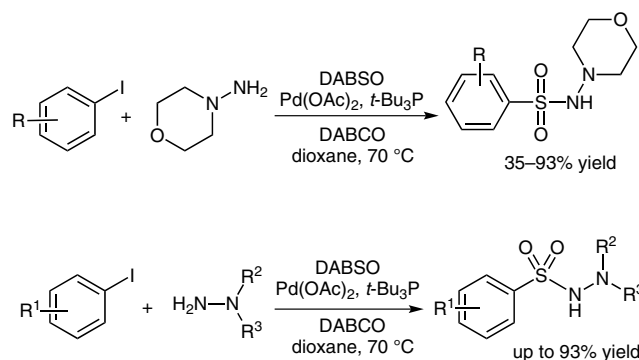
Scheme 1 Synthesis of 1,4-diazabicyclo[2.2.2]octane bis (sulfur dioxide) adduct (DABSO)

Abstracts

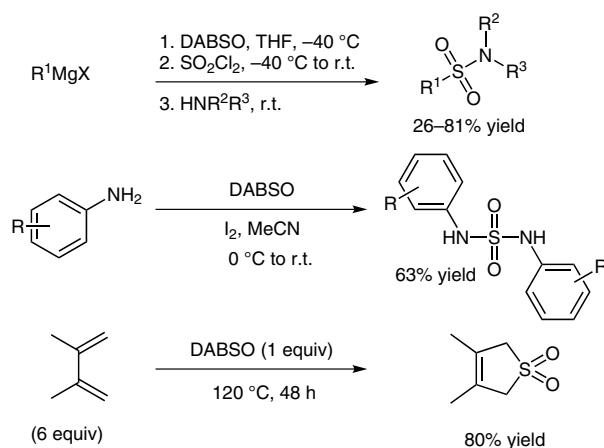
(A) By analogy with already established carbonylation chemistry,^{2a} Nguyen and co-workers^{2b} have demonstrated that it was possible to develop palladium-catalyzed reactions to combine aryl halides, sulfur dioxide and N-nucleophiles. They have shown for the first time that is possible to prepare C–SO₂–N linkages by an aminosulfonylation process using palladium catalysis. With DABSO, the authors achieved aminosulfonylation reactions between a range of aryl iodides and *N,N*-dialkylhydrazines, providing aryl *N*-dialkylaminosulfonamides in good to excellent yield (57–93%).



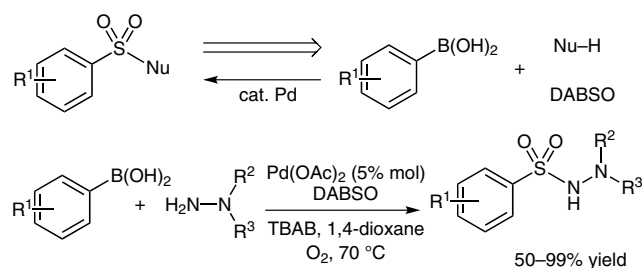
(B) Emmet and co-workers³ have shown that DABSO can effectively replace sulfur dioxide gas in a novel palladium-catalyzed amino-sulfonylation process. For example, 4-iodotoluene and *N*-aminomorpholine in the presence of DABSO, cesium carbonate, *t*-Bu₃P, Pd(OAc)₂ and DABCO in dioxane, yielded the sulfonylhydrazide in 93% yield. Aryl bromides were employed, too, albeit resulting in lower yields. In this report, the authors have extended the scope of the palladium-catalyzed couplings of DABSO with alkenyl and heteroaryl iodides. In addition, other *N*-nucleophiles could be used.



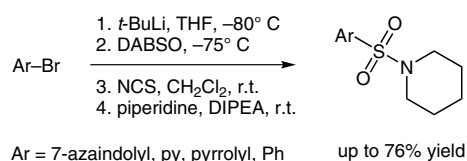
(C) Woolen et al.⁴ have studied the formation of sulfonamides, sulfamides, and sulfolenes. They have demonstrated that DABSO can effectively replace gaseous sulfur dioxide in a number of established processes. One of them consists of preparing sulfonamides from DABSO with aryl Grignard reagents, followed by treatment with sulfonyl chloride and an amine, to afford sulfonamides in good yield. In another example, when DABSO was combined with various anilines and iodine, the authors successfully synthesized several *N,N'*-diphenylsulfamides in 63% yield. They finally established that chelotropic addition of DABSO with 2,3-dimethylbutadiene gives access to sulfolene in 80% yield.



(D) Ye et al.⁵ have developed a novel and efficient route to aryl *N*-aminosulfonamides via a palladium-catalyzed three-component coupling of arylboronic acids, sulfur dioxide and hydrazines in presence of dioxygen. Initially, they studied the palladium-catalyzed reaction of 4-methylphenylboronic acid and *N*-aminomorpholine in the presence of DABSO. Once the ligand, base, solvent and temperature were optimized, they examined a wide range of arylboronic acids and amines under these conditions.



(E) Waldmann et al.⁶ have shown that a bromine–lithium exchange with various aryl halides, followed by addition of DABSO, yields an aryl sulfinate. The authors used DABSO as an alternative SO₂ source in the reaction mixture. With this methodology, they explored a novel application in the synthesis of aryl sulfonamides toward one-pot sequences.



References

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- (3) Emmett, E. J.; Richards-Taylor, C. S.; Nguyen, B.; Garcia-Rubia, A.; Hayter, B. R.; Willis, M. C. *Org. Biomol. Chem.* **2012**, *10*, 4007.
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