Current Organic Chemistry, 2025, 29, 2-18

REVIEW ARTICLE

Cesium Carbonate (Cs_2CO_3) in Organic Synthesis: A Sexennial Update (2018 to Date)

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ARTICLE HISTORY

Received: April 25, 2024
Revised: June 24, 2024
Accepted: June 25, 2024

DOI:
10.2174/0113852728325969240711105055

Abstract Cesium carbonate is an alkali carbonate salt that has numerous applications and has been proven to be a mild inorganic base in organic synthesis. It has garnered significant attention due to its practicality in C-H functionalization and heteroatom-heteroatom bond formation reactions, in addition to its application in conventional synthetic transformations. In this six-year update, we have examined the most important applications of Cs_2CO_3 in organic synthesis from 2018 to the present, including the scope of the reaction and providing detailed explanations of the underlying mechanisms.

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Keywords: Cesium carbonate (Cs_2CO_3), cesium salt, heterocycles, C-H functionalization, heteroatom-heteroatom bond formation, organic transformations, alcohols.

1. INTRODUCTION

Cesium has many great benefits, including short reaction times, little reagent usage, high product yields, gentler reaction conditions, and simple work-up processes, which justifies its greater cost. "Cesium effect" is the term widely used in scientific publications to explain the above-mentioned advantages. The excellent advantage of cesium is mainly attributed to its position in the modern periodic table of elements. Over the past twenty years, there has been a growing interest in the use of cesium salts in various synthetic conversions. Due to its unique properties, which include a high cationic radius (softer Lewis acidity) and easy solvation in a variety of organic solvents, cesium ions have attracted a lot of attention in organic synthesis [1-4]. The application of cesium salts is now accepted in industry. Cesium salts are used, for instance, in palladium-catalyzed coupling reactions, such as the Suzuki coupling and the Buchwald amination reactions. However, since cesium salts have taken the place of conventional bases, they are also used in direct nucleophilic substitution processes.

Cesium carbonate, or Cs_2CO_3, is one of the most important alkaline carbonates of them all [5-8]. Furthermore, cesium carbonate is a well-balanced base that is considered a mild base, and this unique feature is highly essential for selective deprotonation, as well as its suitability for the base-catalyzed reactions, in which it has a basic character weaker than hydroxides or alkoxides and stronger than other carbonates.

There has been a lot of interest in it because of its utility in C-H functionalization, including *C*, *N*, and *O* alkylation and arylation procedures. The effects of cesium salts on intramolecular and intermolecular cyclizations have also been well studied [9-14]. Cesium carbonate not only makes the carbonylation of alcohols and carbamination of amines more efficient, but it also suppresses typical side reactions that are usually encountered with other methods. Varala and co-workers examined the use of cesium salts in organic synthesis and catalysis up till 2015 [15]. Rabie and colleagues examined the numerous applications of Cs_2CO_3 in organic transformations up until the middle of 2017 [16]. This update aims to give a brief overview of the use of cesium carbonate in most noteworthy organic transformations and to highlight its significant contribution to organic synthesis from 2018 onward to date, building on our earlier research and keeping with our focus on the scope of the particular organic transformation and providing detailed explanations of the underlying mechanisms.

2. APPLICATIONS OF CS_2CO_3 IN ORGANIC SYNTHESIS

2.1. Synthesis of Heterocycles

2.1.1. Synthesis of N-substituted Oxazolidinones

Oxazolidinones are important chemical compounds that have a wide range of applications in chemistry and drug discovery. They are used as pharmacophores in the design of biologically active molecules and as chiral auxiliaries in asymmetric organic syntheses, among other functions [17-20]. To investigate and optimize the therapeutic properties of bioactive molecules, one well-established medicinal chemistry technique is the conversion of a primary aliphatic or aromatic amine into an oxazolidinone residue [21]. Kaiser and his colleagues devised a straightforward method for synthesizing oxazolidinone (**3**) using primary aliphatic or aromatic amines (**1**), dibromoethane (**2**, DBE), and either cesium carbonate or cesium hydrogencarbonate as both the base and source of C1, without the need for a catalyst [22]. The broad spectrum of consistently high yields demonstrated the practicality of this technically uncomplicated reaction, enabling rapid modification of amino groups into *N*-substituted oxazolidinones in the late-stage modifications. The optimized reaction parameters of the reaction are: Condition A for 1^{o} aliphatic amines-DBE (2 equiv.), Cs_2CO_3 (3 equiv.) in DMSO (0.122 M) at 25^{o}C, 5 h and Condition B for aromatic amines- DBE (2 equiv.), $CsHCO_3$ (3 equiv.) in DMSO at 50 ^{o}C, 16 h.

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1875-5348/25 $65.00+.00