Introduction

Cesium carbonate is a white hygroscopic powder that is readily soluble in water. It is produced by reacting cesium hydroxide with carbon dioxide1 (Scheme 1).

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2 \text{CsOH} + \text{CO}_2 \rightarrow \text{Cs}_2\text{CO}_3 + \text{H}_2\text{O}
\]

Scheme 1 Preparation of cesium carbonate.

Many of the properties of cesium carbonate are due to the softness of the cesium cation. This softness makes cesium carbonate rather soluble in organic solvents such as alcohols, DMF and Et\text{2}O. This has rendered cesium carbonate useful in palladium chemistry, which is often carried out in non-aqueous media where insolubility of inorganic bases can limit reactivity. \text{Cs}_2\text{CO}_3 has, for example, been used with good results in Heck,2,3 Suzuki4 and Sonogashira5 reactions.

Cesium carbonate has also received much attention for its use in O-alkylations, particularly of phenols.6,7 It has been postulated that O-alkylations of phenols using \text{Cs}_2\text{CO}_3 in non-aqueous solvents occurs via the ‘naked’ phenolate anion, which behaves as a strong nucleophile. Therefore, this methodology can even be applied to secondary halides, minimizing the usual unwanted side reactions such as elimination and decomposition.

Cesium carbonate has also found much use in solid supported synthesis, where solubility can be of importance. It has been reported that it not only promotes successful carboxylation of alcohols and carbamidation of amines, but also suppresses common side reactions traditionally encountered with other protocols.8

In peptide chemistry, a very mild way to produce esters of amino-protected peptides is to treat the carboxylic acid with cesium carbonate followed by the addition of a halide in DMF.9 An intramolecular version has been used to produce macrocyclic lactones.10

Abstracts

(A) Fu and co-workers have used \text{Cs}_2\text{CO}_3 as the base in Suzuki cross-coupling reactions with yields up to 86%. When the same reactions were performed with \text{Na}_2\text{CO}_3 or \text{NEt}_3, the yields were 29% and 50%, respectively.4

(B) Littke and Fu have also shown the superiority of \text{Cs}_2\text{CO}_3 as compared with other bases in the Heck coupling of methylacrylate with chlorobenzene. \text{K}_2\text{CO}_3, \text{NaOAc}, \text{NEt}_3, \text{K}_3\text{PO}_4 and \text{Cs}_2\text{CO}_3 were used to provide yields of only 9%, 21%, 37%, 50% and 56%, respectively.5

(C) In the alkylation of phenols, Parrish and coworkers have shown the utility of \text{Cs}_2\text{CO}_3. Its use makes the alkylation possible even with highly reactive halides which, under other conditions, are prone to eliminations or other side reactions.6

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(D) In natural product chemistry, Fujivara et al. have used Cs₂CO₃ in the key ring-forming step in the synthesis of lipogrammistin-A, originally isolated from the skin mucus of the grammistid fish.¹¹

(E) Salvatore et al. used Cs₂CO₃ when constructing carbonates (not shown) and carbamates in good yield on solid support under CO₂ atmosphere and with TBAI as a co-catalyst.⁸

(F) Walla and Kappe have shown the utility of Cs₂CO₃ as a base when connecting benzoic acids to Merrifield resins under microwave irradiation.¹²

(G) Large macrocycles can be prepared using Cs₂CO₃. The reagent serves both as a base and as a cation template in the macrocyclization of dicarboxylic acids and dihalides to generate the desired crown ethers.¹⁰

References