SYNLETT Spotlight 102

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

Cesium Carbonate (Cs_2CO_3)

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Introduction

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

$$2\ CsOH + CO_2 \longrightarrow Cs_2CO_3 + H_2O$$

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_2O. 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. Cs_2CO_3 has, for example, been used with good results in Heck,[2,3] Suzuki[4] and Sonogashira[5] reactions.

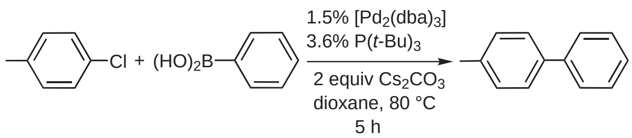
Cesium carbonate has also received much attention for its use in O-alkylations, particularly of phenols.[6,7] It has been postulated that O-alkylations of phenols using Cs_2CO_3 in non-aqueous solvents occurs via the 'naked' phenolate anion, which behaves as a strong nucleophile. Therefore, this methodology 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 carbonylation of alcohols and carbamination of amines, but also suppresses common side reactions traditionally encountered with other protocols.[8]

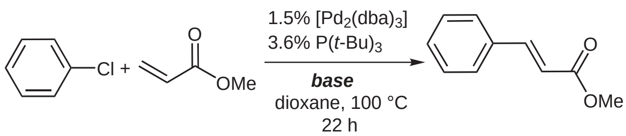
In peptide chemistry, a very mild way to produce esters of amino-protected peptides is to treat the carboxylic acid with cesium carbonate followed by the addition of a halide in DMF.[9] An intramolecular version has been used to produce macrocyclic lactones.[10,]

Abstracts

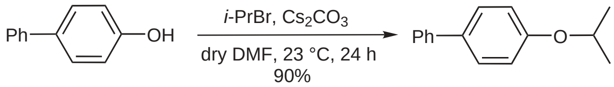
(A) Fu and co-workers have used Cs_2CO_3 as the base in Suzuki cross-coupling reactions with yields up to 86%. When the same reactions were performed with Na_2CO_3 or NEt_3, the yields were 29% and 50%, respectively.[4]



(B) Littke and Fu have also shown the superiority of Cs_2CO_3 as compared with other bases in the Heck coupling of methylacrylate with chlorobenzene. K_2CO_3, NaOAc, NEt_3, K_3PO_4 and Cs_2CO_3 were used to provide yields of only 9%, 21%, 37%, 50% and 56%, respectively.[2]



(C) In the alkylation of phenols, Parrish and coworkers have shown the utility of Cs_2CO_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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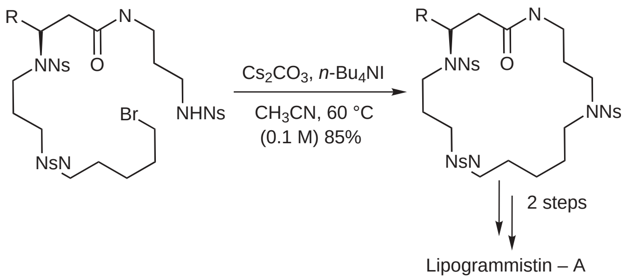
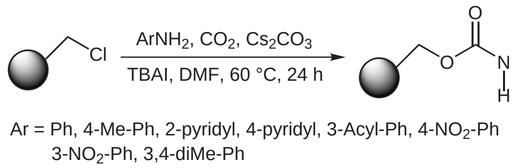
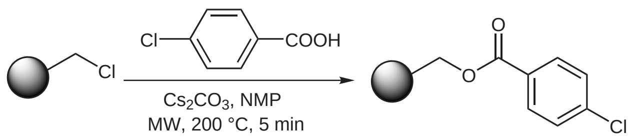
(D) In natural product chemistry, Fujivara et al. have used Cs_2CO_3 in the key ring-forming step in the synthesis of lipogrammistin-A, originally isolated from the skin mucus of the grammistid fish.[11]



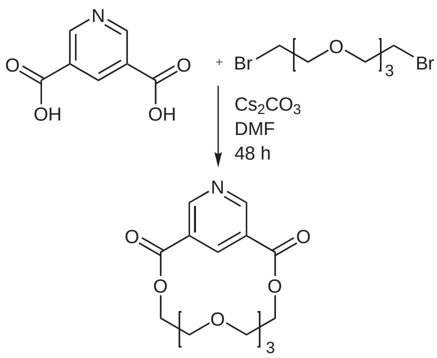
(E) Salvatore et al. used Cs_2CO_3 when constructing carbonates (not shown) and carbamates in good yield on solid support under CO_2 atmosphere and with TBAI as a co-catalyst.[8]



(F) Walla and Kappe have shown the utility of Cs_2CO_3 as a base when connecting benzoic acids to Merrifield resins under microwave irradiation.[12]



(G) Large macrocycles can be prepared using Cs_2CO_3. 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]



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