

SYNLETT Spotlight 36

Di-*tert*-butyl Dicarbonate (Boc-anhydride, Boc₂O)

Compiled by Debendra K. Mohapatra

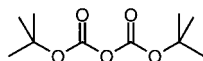


This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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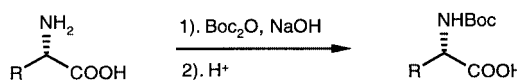
The multifarious role of di-*tert*-butyl dicarbonate (Boc-anhydride, Boc₂O) as protecting group, isocyanating agent, activator of carboxylic acid, lactonisation agent and as a dehydrating agent has been well documented in the records of literature.¹⁻⁸ It is also an efficient *tert*-butoxycarbonylating agent for alcohols, thiols, amines and carbon nucleophiles.⁹ From our group, it has also been exploited as a cyclodehydrating agent for *N*-acylamino acids forming oxazoles and benzoxazinones and as a novel reagent for an efficient synthesis of dipeptides under mild, non-racemizing conditions.¹⁰ It's inexpensive, easy to introduce and cleave as a protecting group, gives innocuous by-products *t*-BuOH and CO₂, and it's mild, and high yielding reaction procedures all add to its value as a versatile and eco-friendly reagent.¹¹



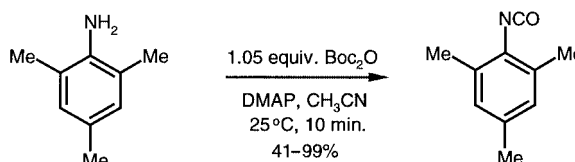
Preparation: Di-*tert*-butyl dicarbonate can be prepared from di-*tert*-butyl tricarbonate and treating with freshly sublimed 1,4-diazabicyclo[2.2.2]octane (DABCO) in carbon tetrachloride at room temperature for 1 hour. The reaction mixture is acidified with aqueous citric acid and the layer is separated. The organic layer is dried over MgSO₄ (anhydrous) and concentrated at 25 °C. The residual oil is distilled under reduced pressure to obtain di-*tert*-butyl dicarbonate (80–91%) as a colorless liquid. The liquid is flammable and must be stored in a refrigerator. It is insoluble in cold water and soluble in most organic solvents.

Abstracts

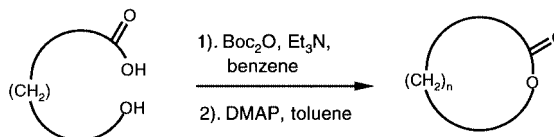
a) Boc-anhydride reacts smoothly with amino compounds in organic solvents or aqueous organic solvent mixtures, to obtain pure *N*-Boc-derivatives in high yields.



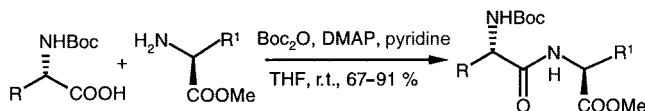
b) Knolker et al. have disclosed a convenient route for the conversion of hindered alkyl and aryl amines into their corresponding isocyanates using Boc-anhydride in the presence of catalytic nucleophilic nitrogen base, especially DMAP. The strategy offers a safe alternative to hazardous phosgene conditions, which is the most widely utilized method for the synthesis of isocyanates.



c) It is also used as a reagent for macrolactonisation of ω-hydroxy acids. The method involves activation of the carboxylic acid by Boc-anhydride, converting it into its mixed anhydride and intramolecular nucleophilic attack of hydroxy group on the activated carbon of the carboxy group forming the lactone.



d) Recently our group has shown that dipeptides can be obtained under mild conditions using Boc₂O as a peptide coupling reagent. The method also eliminates some commonly encountered problems during peptide coupling, such as, separation of product from reagent derived coproduct, racemisation, poor recovery of products, high cost and stability of the reagent etc.



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