

# SYNLETT Spotlight 36

## Di-*tert*-butyl Dicarbonate (Boc-anhydride, Boc<sub>2</sub>O)

Compiled by Debendra K. Mohapatra

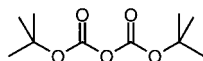


This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Debendra K. Mohapatra was born in Orissa, India in 1970. He did his M.Sc. at Ravenshaw College, Cuttack (Under Utkal University), Orissa, India. He obtained his Ph.D. degree from Indian Institute of Chemical Technology, Hyderabad, India, under the supervision of Dr. Mukund K. Gurjar. Then he moved to University of Texas at Dallas, USA, as a post-doctoral research fellow. Currently, he is working as an associate in the group of Dr. Mukund K. Gurjar at the National Chemical Laboratory, Pune, India.

OCT Division, National Chemical Laboratory, Pune - 411 008, India

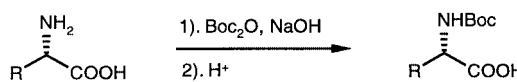
The multifarious role of di-*tert*-butyl dicarbonate (Boc-anhydride, Boc<sub>2</sub>O) as protecting group, isocyanating agent, activator of carboxylic acid, lactonisation agent and as a dehydrating agent has been well documented in the records of literature.<sup>1-8</sup> It is also an efficient *tert*-butoxycarbonylating agent for alcohols, thiols, amines and carbon nucleophiles.<sup>9</sup> 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.<sup>10</sup> It's inexpensive, easy to introduce and cleave as a protecting group, gives innocuous by-products *t*-BuOH and CO<sub>2</sub>, and it's mild, and high yielding reaction procedures all add to its value as a versatile and eco-friendly reagent.<sup>11</sup>



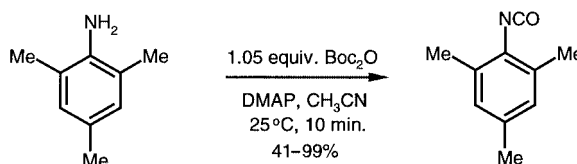
**Preparation:** Di-*tert*-butyl dicarbonate can be prepared from di-*tert*-butyl tricarbonate and treating with freshly sublimed 1,4-diazabicyclo[2.2.2]octane (DABCO) in carbon tetrachloride at room temperature for 1 hour. The reaction mixture is acidified with aqueous citric acid and the layer is separated. The organic layer is dried over MgSO<sub>4</sub> (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

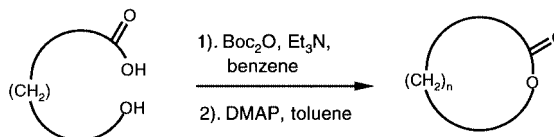
a) Boc-anhydride reacts smoothly with amino compounds in organic solvents or aqueous organic solvent mixtures, to obtain pure *N*-Boc-derivatives in high yields.



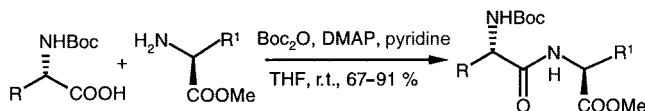
b) Knolker et al. have disclosed a convenient route for the conversion of hindered alkyl and aryl amines into their corresponding isocyanates using Boc-anhydride in the presence of catalytic nucleophilic nitrogen base, especially DMAP. The strategy offers a safe alternative to hazardous phosgene conditions, 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 Boc<sub>2</sub>O 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.



## References

- (1) Tarbell, D. S.; Yamamoto, Y.; Pope, B. M. *Proc. Natl. Acad. Sci. U.S.A.* **1972**, *69*, 730.
- (2) Pozdnev, V. F. *Khim. Prir. Soedin.* **1971**, 384.
- (3) Moroder, L.; Hallett, A.; Wansch, Z.; Keller, O.; Wersin, G. *Z. Physiol. Chem.* **1976**, *357*, 1652.
- (4) Keller, O.; Keller, W. E.; Van Look, G.; Werson, G. *Org. Synth.* **1985**, *63*, 160.
- (5) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, **1991**, 327.
- (6) Kocienski, P. J. *Protective Groups*; Thieme: Stuttgart, **1994**, 194.
- (7) (a) Pozdnev, V. F. *Int. J. Peptide Protein Res.* **1992**, *40*, 407.  
(b) Pozdnev, V. F. *Tetrahedron Lett.* **1995**, *36*, 7115.
- (8) Nagarajan, M.; Kumar, V. S.; Rao, B. V. *Tetrahedron Lett.* **1997**, *38*, 5835.
- (9) Wakselman, M. In *Encyclopedia of Reagents for Organic Synthesis*, Vol. 3; Paquette, L. A., Ed.; John Wiley and Sons: New York, **1995**, 1603.
- (10) (a) Mohapatra, D. K.; Datta, A. *Synlett* **1996**, 1129.  
(b) Mohapatra, D. K.; Datta, A. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 2527. (c) Mohapatra, D. K.; Datta, A. *J. Org. Chem.* **1999**, *64*, 6879.
- (11) Yochai, B.; Hassner, A. *J. Org. Chem.* **2000**, *65*, 6368 and references cited therein.