BOC-ON

Product No.
19,337-2

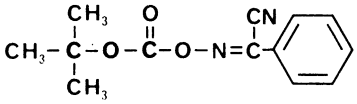
[2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile]

revised 4 / 96 — 4 pages

Technical Bulletin AL-125

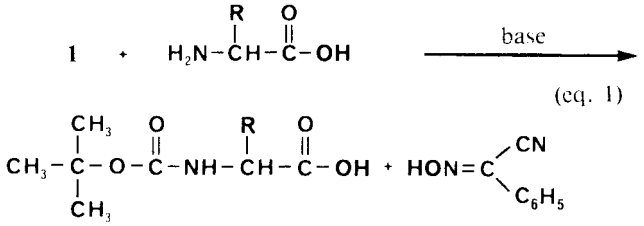
Properties

Molecular formula	$C_{13}H_{14}N_2O_3$
Molecular weight	246.27
Melting point	87-89°C
Solubility	Very soluble in ethyl acetate, ether, benzene, chloroform, dioxane and acetone. Soluble in methanol, 2-propanol and *tert*-butanol. Insoluble in petroleum ether and water.



Application

BOC-ON, 1, reacts simple and rapidly with amino acids to provide protected derivatives in excellent yields (eq.1). *t*-Butoxy-carbonylation of amino acids is carried out at room temperature using a 10% excess of BOX-ON and a 50% excess of triethylamine in either 50% aqueous dioxane or 50% aqueous acetone.



This reagent offers a distinct advantage over *t*-BOC azide which can require reaction temperatures of 50-60°C (*t*-BOC azide is thermally unstable and decomposes with apparent detonation at temperatures above 80°C).[1] The oxime by-product can be easily and completely removed from the reaction mixture by extraction with ether, ethyl acetate or benzene. Deprotection of *t*-BOC amino acids is accomplished under mildly acidic conditions.

The bibliography on page 2 lists references to the use of BOC-ON since its introduction in 1975 by Itoh *et al.*[2] A number of patents to its use in pharmaceutical and agricultural applications have been issued but are not inlcuded in this bibliography.

General Procedure for the Introduction of the *t*-BOX Group into Amino Acids[3]

To a stirred solution of L-tryptophan (2.04g, 10mmol) and triethylamine (2.10ml, 15mmol) (Note 1) is added BOC-ON (2.71g, 11mmol) in a mixture of water (6ml) and dioxane (6ml) at room temperature. The mixture is homogeneous within 1 hour and stirring is continued for 2 hours (Note 2). After addition of water (15ml) and ethyl acetate (20ml), the aqueous layer is separated, washed with ethyl acetate (20ml) (Note 3), acidified with 5% citric acid solution (Note 4) and extracted with ethyl acetate. The dry, concentrated extract gave *t*-butoxycarbonyl-L-tryptophan, 3.00g (98.6%), mp 137-138°C (dec.).

Examples of other *t*-BOC-amino acids prepared by this procedure are shown in Table 1 (Note 5).

Table 1

t-BOX-Amino acids	Reaction time (h)	Oxime extraction solvent	Yield (%)	m.p. (°C)
-Gly-OH	2	EtOAc	86.9	86-88
-Leu-OH•½ H_2O	3	EtOAc	72.0	78-84
-Met-OH•DCHA*	3	EtOAc	82.1	137-139
-Thr-OH•DCHA	3	EtOAc	99.7	151-153
-Phe-OH•DCHA	5	Ether	98.2	221-223

* = dicyclohexylamine

Stability and Storage

BOC-ON should be stored in a brown bottle in the freezer (-20°C) to prolong its shelf life. After several weeks at room temperature, BOC-ON undergoes gradual decomposition with evolution of carbon dioxide.

Toxicity and Handling

Contact with the product may cause irritation. To the best of our knowledge, the chemical, physical and toxicological properties have not been thoroughly investigated. The usual safe laboratory precautions and procedures should be observed when handling this material.

Notes

1• Sodium hydroxide, sodium bicarbonate and other inorganic bases (10 to 15mmol) may be used in place of triethylamine as long as the amino acids are solubilized in the system. In such cases, excess base over 10mmol should be neutralized before the extraction of 2-hydroxyimino-2-phynylacetonitrile to prevent contamination of the *t*-BOC-amino acids.

2• When using a solvent other than dioxane, it is recommended that the solvent be removed before extraction to ensure high yield and purity of the *t*-BOX-amino acid derivative.

3• Other suitable solvents for the extraction of 2-hydroxyimino-2-phenylacetonitrile are benzene and ether. For amino acids with lipophilic side chains, the use of ether is recommended in order to obtain contaminant-free products in high yields.

4• Alternatively, cold 1*N* hydrochloric acid may be used.

5• Dicyclohexylammonium salts are crystallized by the addition of dicyclohexylamine (1.8g per 10mmol amino acid) to an ether solution of t-butoxycarbonylamino acids.[3]

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