Di-tert-butyl Azodicarboxylate

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Introduction

Di-tert-butyl azodicarboxylate (DBAD, 1, Figure 1), also represented as BocN=NBoc, is a yellow crystalline reagent, insoluble in water. It is a light-sensitive compound with a melting point in the range of 90–92 °C.\(^1\)

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\]

Figure 1 Di-tert-butyl azodicarboxylate (DBAD)

DBAD (1) has been widely used for several important reactions and for the synthesis of natural and biological active compounds. Recently, several examples have been published showing the relevance of this reagent in key organic reactions, especially in the α-amination of carboxylic compounds.\(^3\)

Preparation

DBAD (1) is commercially available, but it can be prepared through several methods.\(^1,3,4\) Originally, 1 was synthesized via a two-step reaction involving the preparation of di-tert-butyl hydrazodicarboxylate 2, followed by NBS oxidation of 2 (Scheme 1).\(^1,3\) Recently 1 has been prepared from 2 with pyridine and bromine in dichloromethane.\(^4\)

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\]

Scheme 1 DBAD preparation

Abstract

(A) DBAD (1) is useful in Mitsunobu reactions; generally alcohols are converted into a variety of functional groups in the presence of 1 and Ph\(_3\)P. A recent example is the combined use of polymer-supported triphenylphosphine (PS–Ph\(_3\)P) and 1 to the regioselective coupling of amino acids on the 5′-position of a nucleoside affording the prodrug precursors.\(^5\)

(B) Recently a general route to synthesize ynehydrazides was reported to establish C\(_{sp2}\)-N bonds via addition of in situ generated lithium acetylenes to DBAD (1). This method is useful for the selective synthesis of heterocyclic structures by exploiting both alkyne and hydrazide functional groups in ring-forming reactions.\(^6\)
A Barbier-type propargylation of DBAD (I) with \( \gamma \)-trialkylsilylated propargylic halides, promoted by reactive barium, is a synthetically useful method regarding the regioselectivity affording various propargylic hydrazides in moderate to high yields.\(^1\)

Direct amination of unprotected 3-aryl and aliphatic substituted oxindoles with DBAD (I) in the presence of bifunctional quinine-derived thiourea catalyst is achieved in good to excellent yield and enantioselectivity, establishing a tetrasubstituted stereogenic carbon center at the C3 position of oxindoles.\(^2\)

The direct asymmetric amination of \( \alpha \)-monosubstituted nitroacetates with I and Hatakeyama’s catalyst \( \beta \)-ICD affords \( \alpha \)-aliphatic substituted nitroacetates with high enantioselectivity.\(^3\)