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REVIEW ARTICLE

# Di-*tert*-butyl Peroxide (DTBP)-Promoted Heterocyclic Ring Construction

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**Abstract:** Di-*tert*-butyl peroxide (DTBP) is one of the most widely used organic peroxides in a variety of oxidative transformations. The main factors contributing to the increasing use of DTBP are its affordability, minimal environmental impact, great effectiveness, and capacity to substitute scarce or dangerous heavy metal oxidants. We have reviewed critically and succinctly the noteworthy applications of DTBP in heterocyclic ring constructions from 2014 onwards in this decennial update. The main components of this evaluation are the pros and cons of its use, the scope of a synthetic organic transformation, and mechanistic logistics.



**Keywords:** DTBP, oxidation, organic synthesis, catalysis, heterocyclic ring formation.

## 1. INTRODUCTION

Di-*tert*-butyl peroxide, or DTBP, is an organic molecule composed of a peroxide group linked to two *tert*-butyl groups (Fig. **1**). Because of the large *tert*-butyl groups, it is one of the most stable organic peroxides. At temperatures higher than 100 °C, the colourless liquid experiences homolysis. Because of this, di-*tert*-butyl peroxide is frequently employed in polymer chemistry and chemical synthesis as a radical initiator [1]. Since DTBP serves as both the fuel and the oxidizer in an engine, it is theoretically possible to use it in engines with limited oxygen [2-4].

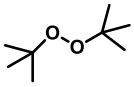


**Fig. (1).** Structure of DTBP.

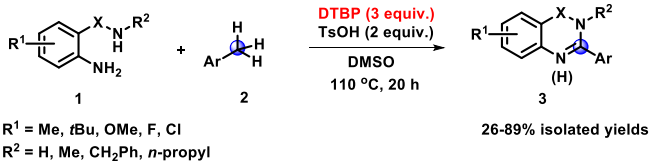
## 2. APPLICATIONS OF DTBP IN HETEROCYCLIC RING FORMATIONS

### 2.1. Quinazolinones

#### *2.1.1. Synthesis of 2-aryl Quinazolinones (via Dual Amination)*

Heterocycles containing nitrogen are found in a great deal of natural products and drugs. Quinazolinone heterocycles have been the subject of much research because of their biological and therapeutic properties [5-16]. Li and his research team developed a unique metal-free synthesis of quinazolinones **3** by dual amination of $sp^3$ C-H bonds [17]. The one-carbon synthon was the $sp^3$ carbon found in methylarenes or next to a heteroatom in DMSO, DMF, or DMA. *The optimized reaction conditions are*: TsOH (2 equiv.), DTBP (3 equiv.) in DMSO at 110 °C, 20 h. Control experiments on 2-amino benzamide and toluene revealed that DTBP (81% isolated yield) was the most efficient one compared to other oxidants such as TBHP (trace), BPO (45%), TBPB (36%) DDQ (NR) and $K_2S_2O_8$ (NR).

Then, under optimized conditions, a variety of 2-amino benzamides **1** were used for annulation with methylarenes **2** (Scheme **1**). In moderate to good yields, the majority of toluenes with substituents that donate electrons and withdraw them could be transformed into the intended products **3**. Surprisingly, the reaction was not much affected by the steric hindrance. Heteroarene and naphthalene replaced with methyl also turned out to be useful. The effectiveness of this transition was unaffected by the substituents at the phenyl ring of 2-amino benzamides. This method might also be used to create quinazolinones with *N*-phenyl and *N*-alkyl substituents by reacting toluenes with corresponding 2-amino *N*-substituted benzamide. When 2-amino benzenesulfonamide was examined due to the structural similarity, 3-phenyl-3,4-dihydro-(2*H*)-1,2,4-benzothiadiazine-1,1-dioxides were produced as byproducts. The reduced yields compared to quinazolinones were most likely caused by low nitrogen nucleophilicity of sulfonamides. The authors also attempted but were unsuccessful, to construct fused four-membered rings *via* an intramolecular process.




**Scheme 1.** Intermolecular annulations of **1** with methylarenes **2**.

Following their successful elaboration of 2-substituted quinazolinones, the authors redirected their attention to the potential of dimethylacetamide (DMA) as a viable carbon source. Beginning with substrates that had *N*-aryl, *N*-alkyl, or phenyl substituents, the intended products **4** were produced with moderate to good yields, as shown in Scheme **2**. Remarkably, functional groups like F, Cl, or Br remained intact, enabling the products to be further functionalized.

As illustrated in Scheme **3**, a potential mechanism is suggested. DTBP homolysis first produced *tert*-butoxy radicals. After that, H was abstracted from toluene to form the benzyl radical, and the two

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