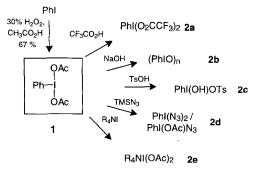
# (Diacetoxyiodo)benzene DIB - a Multitalented Oxidant in Organic Synthesis

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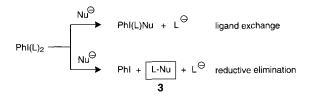
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Organic compounds of polycoordinated iodine have long been known. In fact, in 1886 Willgerodt [1] presented the first preparation of PhICl<sub>2</sub> from iodobenzene and ICl<sub>3</sub> in this journal! Only recently iodine compounds in the oxidation state III have gained synthetic and mechanistic significance, as described in numerous recent reviews [2]. This renewed interest was initiated by the development of various new iodine(III) reagents  $2\mathbf{a} - \mathbf{d}$ as well as iodate(I) salts  $2\mathbf{e}$  which in most cases can conveniently be prepared *in situ* from a common iodine(III) precursor, *i. e.* (diacetoxyiodo)benzene DIB (1) (Scheme 1) [3].





The strongly electrophilic character of hypervalent iodine is mainly responsible for its diverse chemistry. The reactivity pattern of 1 and other iodine(III) reagents is briefly summarized in Scheme 2. It is primarily based on ligand exchange reactions and reductive elimination of two ligands on the central iodine atom. In most cases, reactions of 1 with nucleophiles are terminated by the second route, affording final products 3 with a combination of L and Nu. Due to this behaviour compounds like 1 are occasionally termed "nonorganometallic" reagents.



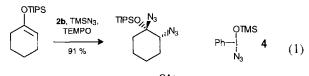


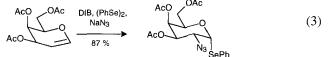
As will be shown, the breaking of the I–L bond can occur hetero- or homolytically.

For successfully introducing a new reagent or reaction on the "market" of preparative organic chemistry today, it is important that the conversion described is highly stereo-, regio- and as has often be forgotten chemospecific. Unfortunately, most reviews on iodine(III) [2] have not addressed this point in great detail. It is therefore the intention of this brief report to present recent uses of iodine(III) reagents like 1 or reagents derived from it in reactions with complex multifunctional substrates and in natural product synthesis.

### **1** 1,2-Additions to Olefines

DIB (1) can be used to promote 1,2-addition reactions to olefines. However, 1 is only able to transfer acetoxy groups to highly nucleophilic alkenes and cyclopentadiene [4]; isolated double bonds are inactive under mild conditions. Over the last years various procedures have been developed, where 1 is used to activate other heteroatom containing reagents, which then add to olefinic double bonds (Scheme 3). Triisopropylsilyl enol ethers are ideally suited for bisazidonation under radical conditions (equ. 1) [5]. The authors propose that iodine(III) intermediate 4 adds to 2,2,6,6-Tetramethylpiperidin-1-oxyl ("TEMPO") to give an I(IV) species which is able to generate azide radicals.  $\alpha$ -Acetoxy iodides have been prepared from indene by utilizing novel iodate(I) salts like 5 (see also Scheme 1; analogous to 2e) [6]. These are



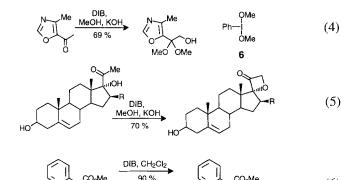




prepared by ligand transfer from 1 onto the iodide source (equ. 2). An interesting 1,2-addition to olefines, which is initiated by 1, has been developed by Tingoli *et al.* and later applied in carbohydrate chemistry [7]. Thus, glycals are transformed into 2-azido-pyranosyl selenides in one step (equ. 3). In the primary step the authors postulate iodine(III)-initiated formation of the azide radical which adds to the olefinic double bond. In the following, the newly generated C-radical is trapped by diphenyl diselenide.

### 2 $\alpha$ -Functionalization of Ketones

Iodine(III) oxidation of enolizable ketones using DIB (1) in methanolic KOH provides one of the best methods for  $\alpha$ oxidation of ketones. It is generally accepted that **6** acts as the active intermediate. After coupling with the enolate anion a cascade of reactions is initiated which eventually leads to  $\alpha$ hydroxydimethylketals (Scheme 4, equ. 4) [8]. Intramolecular variants of this process have been used for constructing steroidal oxetanes from the corresponding 17-hydroxy-17acetyl precursors (equ. 5) [9]. In few cases, **1** has been employed in the  $\alpha$ -acetoxylation of ketones (equ. 6) [10].



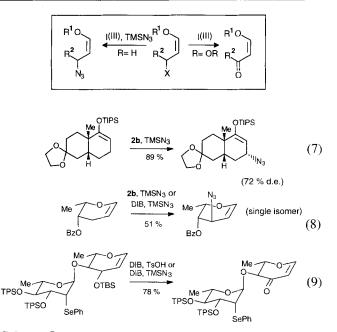
#### Scheme 4

## 3 Allylic Oxidation of Olefines

In recent years the iodine(III)-promoted allylic oxidation of electron-rich olefinic double bonds, particularly of carbohydrate derived glycals and triisopropylsilyl enol ethers have been studied in detail (Scheme 5). This type of conversion reveals a unique reactivity pattern of polycoordinated iodine compounds and is assumed to proceed *via* an ionic addition/ elimination mechanism [11]. In these examples DIB (1) was used for *in situ* generation of iodine(III)-reagents **2c** and **2d**. These were employed for azide transfer onto the allylic position (equ. 7 [12] and 8 [13]) or for the allylic oxidative deblocking of glycals (equ. 9) [14].

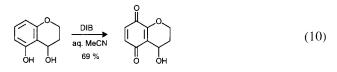
# 4 Phenolic Oxidation

1 has widely been employed in the oxidation of simple and complex phenols. Depending on the substrate and the conditions used, dehydrogenation, oxygenation and oxidative





addition with carbon–carbon or carbon–oxygen bond formation can occur (Scheme 6). *E.g.* phenols with weakly acidic character can directly be converted into quinones (equ. 10) [15]. Alternatively, this process can be exploited for intramolecular phenolic C–C coupling, which has found numerous applications in alkaloid chemistry (equ. 11) [16].





Scheme 6

(6)

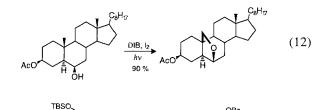
# 5 Photochemical Activation of Alcohols

Reaction of **1** with iodine in the presence of alcohols under photochemical conditions can lead to the generation of alkoxy radicals (Scheme 7). Depending on the nature of the remaining functionalities present in the substrate, cyclizations or fragmentations can occur in the following. Applications of this reaction are widely found in steroidal (equ. 12, Scheme 8) [17] as well as carbohydrate chemistry (equ. 13) [18]. Recently, Danishefsky and coworkers employed the Suárez oxidation for the construction of the C28-C42 segment of rapamycin (equ. 14)[19].

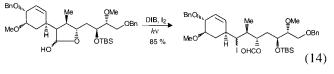
(11)

$$\frac{hv}{AcOl} \xrightarrow{ROH} AcOH + ROI \xrightarrow{hv} RO^{\bullet} + I^{\bullet}$$

#### Scheme 7









#### **6** Miscellaneous

This short report can only cover some aspects of the rich chemistry of (diacetoxyiodo)benzene (1). Many other applications are known of which the following are particularly worth mentioning, as they have also found use in reactions with multifunctional substrates. In the presence of 1 and in particular [bis(trifluoroacetoxy)iodo]benzene (2a) primary carboxamides, including peptide amides undergo facile Hofmann-type rearrangement affording amines in high yield [20]. 2a has proven to be a very mild and efficient reagent for the dethioacetalization of dithiaacetals thereby generating the corresponding aldehydes [21]. Finally, iodine(III) reagents derived from 2b have been used as promotors in glycosidation reactions with thioglycosides [22].

From these few examples presented here, it is obvious that DIB (1) promotes a rich and diverse chemistry. As the number of reagents that derive from 1 further increase, the importance of hypervalent iodine in preparative organic chemistry will further enhance.

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more, **2a** and **2c** can also be obtained from Aldrich and Fluka

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