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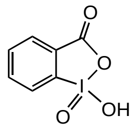
[15] See ref. [1–3] for discussion of values; see also: O. Gonzalez-Blanco, U. Branchadell, *J. Chem. Phys.* **1999**, *110*, 778. It is interesting that calculations in ref. [3] suggest an energy of interaction between ^{1}**4** and $\mathrm{C_2H_6}$ of about 7 kcal mol^{-1}, and a ^{1}**4**/^{3}**4** gap of about 6 kcal mol^{-1}. On this basis, the solvent-stabilized singlet $[\mathrm{Fe(CO)_4}]$ (i.e. ^{1}**4** · solvent), has approximately the same energy as ground-state triplet $[\mathrm{Fe(CO)_4}]$ (i.e. ^{3}**4**).

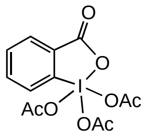
IBX—New Reactions with an Old Reagent

Thomas Wirth*

Hypervalent iodine reagents have attracted increasing interest during the last decade because of their selective, mild, and environmentally friendly properties as oxidizing agents in organic synthesis.[1] 2-Iodoxybenzoic acid (IBX, 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **1**) was first reported in 1893[2] but has been rarely used in reactions, probably due to its insolubility in most organic solvents.[3] Dess and Martin transformed IBX (**1**) into the much more soluble Dess–Martin periodinane (DMP, 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one **2**),[3, 4] which has received much attention. Improved procedures for the synthesis of reagents **1** and **2** have been disclosed recently.[5–7]

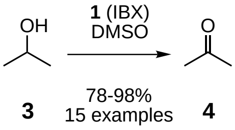


1 (IBX)

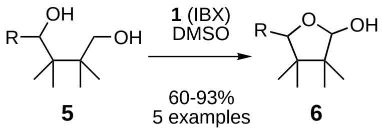


2 (DMP)

The broad functional group tolerance of these reagents and high-yielding reactions without over-oxidation have made DMP (**2**) very prominent for the oxidation of alcohols to the corresponding carbonyl compounds. But IBX (**1**) in DMSO was also found to be a highly efficient reagent for the clean oxidation of alcohols **3** to carbonyl compounds **4** even in the presence of thioethers or amines[8, 9] (the number of reported examples are given below the arrows here and in the following). It is also possible to selectively oxidize 1,2-diols to 1,2-diketo derivatives without oxidative cleavage of the glycol C–C bond.[8, 10] The selective oxidation of 1,4-diols **5** to the corresponding γ-lactols **6** can also be realized.[11, 12]



3 **4**



5 **6**

The first step in these oxidation reactions is a fast pre-equilibrium, which can be formally considered as ligand exchange (hydroxy–alkyloxy) on the iodine atom. The product **7** then disproportionates to the carbonyl derivative **4** and the iodosoarene **8** (IBA).[10]

The known paths for the oxidation of alcohols have been extended by recent reports utilizing IBX (**1**) and DMP (**2**)[13] in other transformations. The introduction of an α,β-double bond into carbonyl compounds is sometimes a challenging transformation, which is predominantly performed by using selenium or palladium reagents. A ligand exchange on IBX with the ketone-enolate might be involved in the key step in the mechanism of this new and general procedure. Although the reaction proceeds only at elevated temperatures (65–85 °C), even acid-labile carbonyl compounds can be employed in the process, from which derivatives **9** are obtained in good

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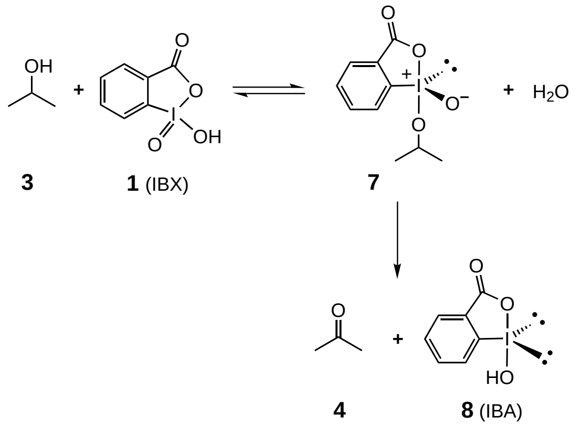
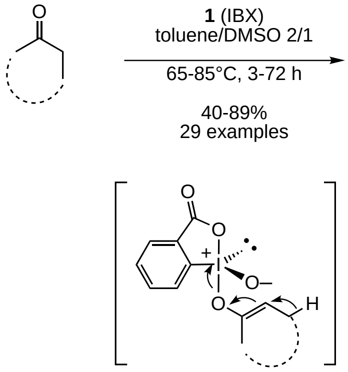
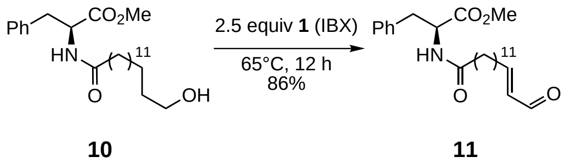


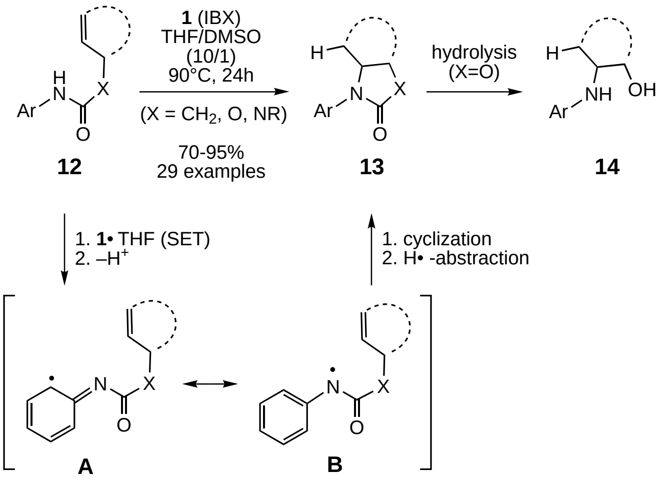
yields.[14] Even alcohols can be converted to α,β-unsaturated carbonyl compounds directly by using an excess of IBX (**1**), as shown in the oxidation of the phenylalanine derivative **10** to **11**.



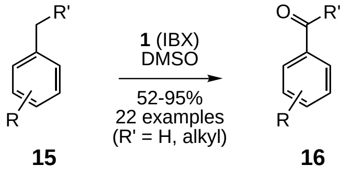


Although hypervalent iodine compounds are often used as oxidants and sometimes as electrophilic reagents, the cyclization of aryl-substituted unsaturated amines to heterocycles **13** is started by a single-electron transfer (SET) reaction. Either **1** or an IBX·THF adduct serves as the oxidant to initiate the heterocyclization by a SET process. The subsequently generated N-centered radical will then cyclize in a 5-*exo-trig* manner to yield, after hydrogen abstraction from the solvent, heterocycles of type **13**. The cyclization of amides to γ-lactams offers the possibility to synthesize even a variety of annelated heterocyclic compounds. The IBX-mediated cyclization of (thio)carbamates and ureas to (thio)oxazolidinones and cyclic ureas can be followed by hydrolysis to synthesize, for example, 1,2-amino alcohols of type **14**.[15] The fast access to the carbamate starting materials by adding allylic alcohols to isocyanates allows the rapid generation of compound libraries.[16]

The mechanism of this transformation has been investigated in detail. Although amide radicals have already been employed in cyclization reactions,[17] their involvement in the IBX-mediated reaction has been proven by a detailed analysis.[15b] It was concluded that the irreversible SET from the aryl moiety to the IBX·THF adduct is the rate-determining step of the reaction and can only proceed with a free *ortho*-position in the substrate as shown in the mesomeric structures **A** and **B**.

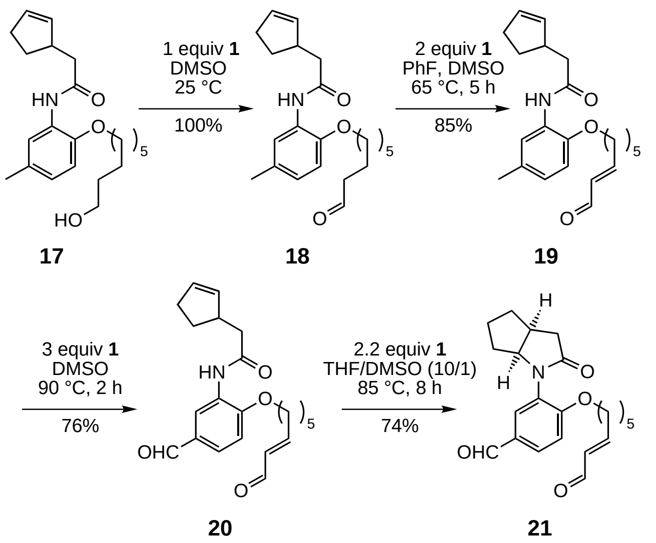


On the basis of this reaction mechanism, a process for the oxidation of the benzylic position has been developed recently. This reaction is quite general and proceeds with an excess of **1** at higher temperatures. Over-oxidation of compounds **15** with R′ = H to the corresponding carboxylic acids was not observed, and the yields of ketones or aldehydes **16** even with labile substrates were generally quite high.[18]



To show the selectivity and controllability of these IBX-mediated reactions, substrate **17** was synthesized and converted in a series of steps to compound **21**. The cyclization reaction **20**→**21** must not necessarily be the last step in the sequence.

As shown recently in the hydrolysis of phosphonofluoridates, **1** can also be used as a catalyst with oxone being the stoichiometric oxidant.[19] IBX (**1**) is able to oxidize thiols selectively to the corresponding disulfides.[20] It can also be used as a versatile reagent for the cleavage of oximes and tosylhydrazones to the corresponding carbonyl compounds.[21] The first attempts to synthesize chiral reagents derived from IBX have appeared, although the selectivities obtained in the sulfide oxidation are low (up to 16% *ee*).[22] The development of electronically modified IBX reagents[23] to tune electron



transfer processes, their application to new reactions, and the synthesis of polymer-bound IBX[24] for rapid combinatorial chemistry will undoubtedly be reported in literature in the near future.

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