A Stable and Safe Form of Iodine Azide: Polymer-Bound Bisazido-iodate(I)

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While haloazides like iodine azide have been known for many years, their use in synthetic organic chemistry has been considered challenging due to their unstable or even explosive nature. Due to the extraordinary versatility of these interhalogen reagents for synthetic chemistry, there is a fundamental demand for safe and easy-to-use substitutes.

Although IN₃ can be generated in situ from iodine chloride and sodium azide in polar solvents, this method and similar routes from TIN₃ or Bu₃SnN₃ have not gained wide acceptance. A safe route for the formation of IN₃ in the form of a stable analogue, the bisazidiodate(I) complexes 3 or 3′, which can be generated from organic iodide sources such as tetraalkylammonium iodide 1′ or basic ion-exchange resin, is reported. The first step represents the oxidation of iodide, mediated by iodine(III) reagents, and the resulting iodate(I) complexes 2 or 2′ are then subjected to a ligand exchange reaction with Me₃SiN₃ to form the bisazidiodate(I) complexes 3 or 3′ (Scheme 1). While the ammonium-bound complex must be prepared in situ, a polymer-assisted version can be prepared on a large scale and stored for several months under argon atmosphere at −15 °C without loss of activity. The polymer did not exhibit explosive properties in impact experiments. Reactions with these functionalized polymers can be terminated by simple filtration. Active reagents remaining in solution can subsequently be removed by workup with thiosulfate-loaded ion-exchange resin, eliminating the need for aqueous workup. Filtered polymeric byproducts such as 4 can be used to recover the iodide loaded exchange resin 1 from where polymer-bound reagent 3 can be regenerated.

It has been suggested that iodine azide is released into solution from the polymer-bound bisazido iodate(I) complex 1 into the organic solvent of choice. There it can undergo a variety of reactions under well-controlled conditions. With alkenes, 1,2-addition is usually observed, yielding the corresponding 2-iodoazides. Noteworthy, these reactions tolerate various other functional groups and, in combinations with other functionalized polymers such as polymer-bound 1,8-diazabicyclo (5.4.0)undec-7-ene (DBU) 6, could

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be used as chemically active fixed-bed materials inside flow reactors (Table 1, A).

If these reaction mixtures are irradiated with light, e.g., using blue LEDs, a drastically changed reactivity is observed. Iodine azide is then no longer characterized by the electrophilicity of iodine, but radicals now dominate the reaction events. This includes the formation of radical addition products. Problems arising from the photoinstability of the carbo–iodine bond formed can be circumvented by addition of a stable radical scavenger such as (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO). This results in azido-oxygenated products from alkenes. In contrast, sterically very demanding substrates are oxidatively converted into bisazido adducts (Table 1, B).

In this way, iodine azide can not only be added to double bonds, but the photochemically generated azide radical can abstract hydrogen atoms from secondary alcohols to form intermediate ketyl radicals. The second H-abstraction then terminates the oxidation of the secondary alcohol and ketones are formed. The chemoselectivity of this oxidation is particularly noteworthy because it leaves primary alcohols unaffected (Table 1, C).

Under forcing conditions, however, primary alcohols also react, presumably to form aldehydes, which then undergo further H-abstraction under the photochemical conditions, and in that case the acyl radical is scavenged by the N₃ radical and acyl azides are formed, which further rearrange to the carbamoyl azide by Curtius rearrangement (Table 1, D).

### Table 1 Applications of Polymer-Bound Bisazidoiodate(I) Complex 3 and a Stable Form of IN₃

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<th>Scheme 1 Preparation of iodate(I)-based IN₃ analogue 3 and regeneration from byproduct 4 via 1; ion-exchange resin 5 suitable for reductive workup of reactions with 3 (R = polystyrene 1, 2, 3 or alkyl 1′, 2′, 3′). The photograph of 3 displays the orange color of the resin.</th>
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<td><strong>(A)</strong> The addition of 3¹³ to alkenes will result in electrophilic addition, forming the 1,2-anti-iodoazidated product. A large variety of functional groups, such as alcohols, nitro groups, and pyridines, is tolerated.² Further treatment with non-nucleophilic bases such as DBU can induce the elimination of hydrogen iodide towards the newly introduced azide group. This was reported for a telescoped flow protocol.³⁴⁵</td>
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<td><strong>(B)</strong> The addition of iodate(I) complex 3¹³ to alkenes under irradiation conditions using blue LEDs results in the formation of the 1,2-bisazido addition product. However, the intermediate C-radical formed can be trapped with TEMPO to furnish the anti-azido-oxygenated product.¹ Sterically demanding alkenes preferentially still furnish 1,2-bisazides under these conditions.</td>
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In addition, polymer-bound bisazidoiodate(I) 3 provides a phenol-oxidation chemistry more familiar with iodine(III) compounds. para-Substituted phenol derivatives are achieved with polymer 3.\textsuperscript{5,15} Exposure of phenol to 3 results in 2,4,6-triiodophenol (not shown).

Finally, activated positions such as benzylic or α-carbonyl positions can be azidated when heated in the presence of the functionalized polymer 3 (Table 1, F and G).

In summary, bisazidoiodate(I) complexes enable a variety of diverse reactions and functionalizations that include alkene bifunctionalizations, alcohol and phenol oxidations. As a polystyrene-supported reagent, it offers additional advantages over homogeneous reagents in terms of stability, ease of workup, recycling (see Scheme 1), and thus reduction of waste. Due to its highly increased safety profile compared to iodine azide, a broader use of reagent 3 can be expected in the future, which will reveal additional reactivity of the very versatile interhalogen reagent IN\textsubscript{3}.

Conflict of Interest

The authors declare no conflict of interest.

References and Notes

11. Preparation of Polymer-Bound Bisazidoiodate(I) 3

Amberlyst® A26 resin (4.2 mmol/g hydroxide form) was sequentially rinsed with 1 M NaOH (4 mL g\textsuperscript{-1} polymer), saturated Li solution (5 mL g\textsuperscript{-1} polymer), distilled water (4 mL g\textsuperscript{-1} polymer), isopropanol (4 mL g\textsuperscript{-1} polymer), and CH\textsubscript{2}Cl\textsubscript{2} (4 mL g\textsuperscript{-1} polymer). A suspension of this polymer and Ph(OAc)\textsubscript{2} (1.8 equiv) was shaken in dry CH\textsubscript{2}Cl\textsubscript{2} (3 mL g\textsuperscript{-1} resin) at 85 °C for 18 h at room temperature under an argon atmosphere. During this time, the mixture was protected from light. The pale-yellow resin 2 was filtered, washed with CH\textsubscript{2}Cl\textsubscript{2} (30 mL g\textsuperscript{-1} resin), and dried in vacuo. The polymer can be stored for several
months under argon atmosphere at –15 °C in the dark without loss of activity. Subsequently, a suspension of this functionalized ion-exchange resin 2 (4.2 mmol anion g⁻¹ resin, 1.0 equiv) and trimethylsilyl azide (2.6 equiv) in dry CH₂Cl₂ (4 mL/g resin) was shaken at 665 rpm for 6 h at room temperature in the absence of light under an argon atmosphere. The orange resin 3 was filtered, washed with CH₂Cl₂ (30 mL g⁻¹ resin), and dried in vacuo. In practice, an effective loading of up to 2.1 mmol of reagent g⁻¹ of resin can be achieved. It can be stored for several months under argon atmosphere at –15 °C in the dark without loss of activity.

(12) It is worth noting that polymer 3, after being evaluated as safety, was commercially available for several years in the early 2000s.

(13) Note: The number of equivalents for 3 refers to the theoretical loading as specified by the manufacturer of the ion-exchange resin. The actual amount of IN₃ available is much less, therefore the number of equivalents does not describe the true ratio.