Iodine Monobromide

[7789-33-5] BrI (MW 206.80)

InChI = 1S/BrI/c1-2

InChIKey = CBEQRNSPHCCXSH-UHFFFAOYAO

(diastereoselective cyclizations of homoallylic carbonates;[1] electrophilic addition to alkenes;[2] α-bromination of steroidal aldehydes and ketones;[3,4] cleavage of carbon–metal bonds[5])

Physical Data: mp 40 ° C; bp 116 °C (dec); *d* 4.416 g cm^{-3}.

Solubility: sol alcohol, ether, CS_2, acetic acid, acetone, CH_2Cl_2, MeCN, DME, toluene (but with limited solubility below −80 °C); soluble in H_2O, but hydrolyzes to HBr and IOH.

Form Supplied in: brownish-black crystals or very hard, black solid; widely available (usually 97–98% purity).

Handling, Storage, and Precautions: corrosive solid and vapor; readily absorbed through skin and mucous membranes; use in a fume hood and wear gloves and appropriate protective clothing; air-, moisture-, and light-sensitive; should be stored refrigerated (under N_2) in a tightly sealed amber bottle. Forms explosive mixtures with potassium and sodium, and reacts extremely exothermically with phosphorus and tin.

Original Commentary

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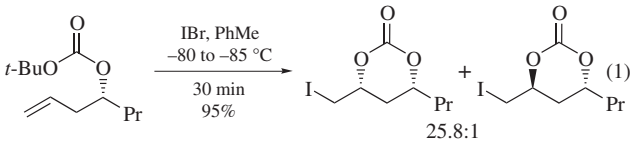
Electrophilic Cyclization of Homoallylic Carbonates.[1] Iodine monobromide provides very good diastereoselectivity in electrophilic cyclizations of homoallylic carbonates (eq 1). Isolated yields of α-iodo cyclic carbonates are excellent, and these products can be easily and efficiently converted into the corresponding epoxides (eq 2). Optimal diastereoselectivity is obtained from reactions performed in toluene at −80 to −85 °C. Use of ***Iodine***/MeCN[6] or ***Iodine Monochloride***/CH_2Cl_2 yields much lower diastereoselectivity than iodine monobromide under similar conditions. Results of an equilibration experiment strongly indicate that the diastereoselectivity in iodine monobromide-induced cyclization stems from kinetic control.

Electrophilic Addition to Alkenes.[2] Iodine monobromide addition across alkenes is very facile, yielding vicinal bromoiodoalkanes. In general, addition occurs with high *anti* stereospecificity, and mechanistic studies have implicated an iodonium ion intermediate in the overall reaction sequence. The regiochemistry of iodine monobromide addition is very sensitive to the initial alkene structure, such that anti-Markovnikov products are possible (Table 1).



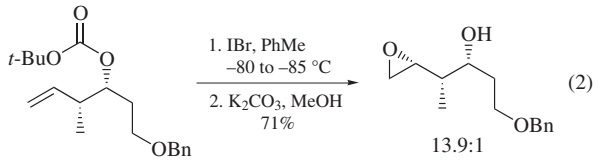
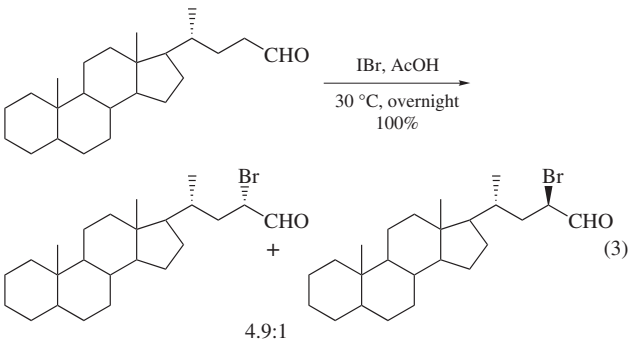


Table 1 Regiochemistry of IBr addition to alkenes

Alkene	% Markovnikov	% anti-Markovnikov
$MeCH{=}CH_2$	65	35
$ErCH{=}CH_2$	45	55
i-$PrCH{=}CH_2$	15	85
t-$BuCH{=}CH_2$	0	100
$PhCH{=}CH_2$	100	0

α-Bromination of Steroidal Aldehydes and Ketones. Iodine monobromide is an effective monobrominating reagent for steroidal aldehydes (eq 3).[3] The ratio of diastereomeric products is in part a function of the reaction site's proximity to an asymmetric center, with β-orientation favored for the entering bromine. In an analogous application, methyl 3-oxo-5β-cholanate has been monobrominated (IBr/$MeCO_2H$; 50% yield) to produce the 2β-bromo ketone.[4]



Bond Cleavage Reactions.[5] Cleavage of carbon–metal bonds by iodine monobromide typically produces the organic iodide and the metal bromide. Cleavage of organotin,[5a–c] organoarsenic,[5d] organoantimony,[5d] organogermanium,[5e] and organolead[5e] bonds has been investigated (see also ***Iodine Monochloride*** for use in cleaving carbon–metal bonds).

Other Applications. Iodine monobromide has been used for brominating phenol and aryl ether derivatives.[7] Ethers and esters have been cleaved by catalytic iodine monobromide in the presence of ***Bromotrimethylsilane***.[8] Aryl acetals can be directly oxidized to the corresponding esters in moderate yield.[9]

First Update

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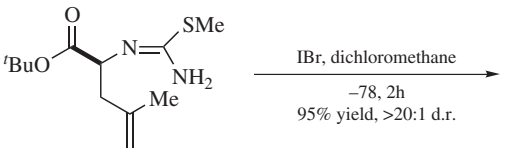
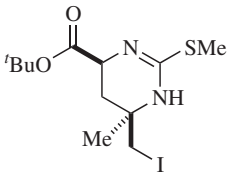
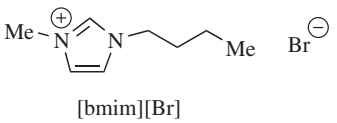
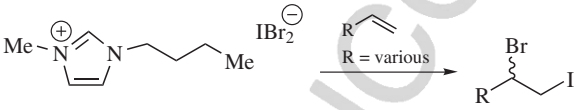
Electrophilic Cyclization. Iodine monobromide continues to be exploited in stereoselective cyclization reactions *en route* to natural products, such as calyculin[10] and halichondrin B.[11] It can also be employed in diastereoselective isothiourea iodocyclization reactions, which proceed smoothly using IBr at low temperature. Advanced intermediates in the synthesis of manzacidin A, amongst other examples, have been obtained using this procedure (eq 4).[12]




(4)

Electrophilic Addition to Alkenes. Trihalide-based ionic liquids, produced by mixing equimolar amounts of IBr and [bmim][Br], prove to be effective reagent-solvents for stereoselective iodination of alkenes and alkynes.[13] Yields of iodobromo adducts range from very good to almost quantitative for a range of substrates (eq 5).

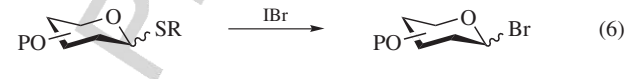




(5)

Formation of Glycosyl Bromides. Iodine monobromide is used for the synthesis of glycosyl bromides from various alkyl and aryl thioglycosides (eq 6).[14] The reaction of IBr with thioglycosides is compatible with many of the common protecting groups, such as isopropylidene acetals, cyclohexane 1,2-diacetals, 4-methoxybenzyl and benzyl ethers, phthalimido groups, etc. Compounds containing intersugar glycosidic linkages form glycosyl bromides at their reducing terminal only, without affecting existing glycosidic linkages.

Glycosylation Chemistry. Iodine monobromide is an efficient reagent for *O*-glycosylation using "disarmed" thioglycoside donors.[14,15] It provides excellent 1,2-*trans* stereoselectivity and it is compatible with most common protecting groups and existing *O*-glycosides. However, issues can arise from the Lewis acidity of IBr, which can effect acyl migration. In addition, competing glycosyl bromide formation may have an impact on reaction outcome.[15] These problems can largely be overcome through the use of IBr in conjunction with silver triflate. Studies on interhalogen/silver trifluoromethanesulfonate (IX/AgOTf) promoted glycosylations reactions identified differences in the sensitivity of the formed oxocarbenium ions, e.g., from compounds with or without participating groups) toward halide nucleophiles.[16] These differences can be explained using the Hard-Soft-Acid-Base theory. By applying this theory silylation yields were increased for a model reaction from ~40% using ICl to 74% using IBr. By increasing the amount of AgOTf from 1 to 1.5 equiv (with respect to IBr) the yield in the model reaction improved to 89%, with a move from xanthate to thiophenyl glycoside donor further increasing the yield of the model reaction to 97% (eq 7).



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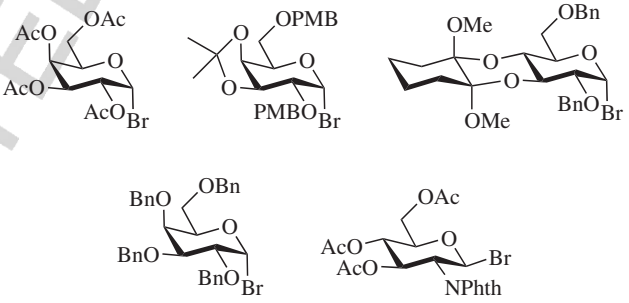

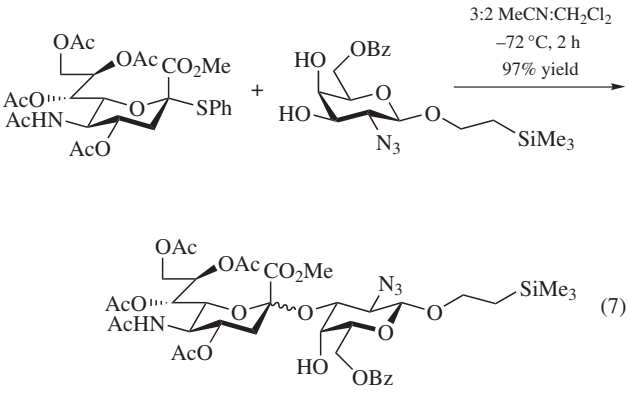

(7)

Other Applications. Iodine monobromide has been used as a mild reagent for selective deprotection of *O*-*tert*-butyldimethylsilyl ethers of simple alcohols, carbohydrates, and nucleosides.[17] Acid labile functionalities such as acetals, *O*-*p*-methoxybenzyl ethers, etc., as well as base labile esters and amides, are stable in the presence of iodine monobromide. Among several solvents used for the reaction, methanol gives the best yields, which may indicate that desilylation is a result of in situ generation of HBr.

Radical addition of iodine monobromide to chlorotrifluoroethylene forms a useful intermediate in the synthesis of 4,5,5-trifluoro-4-ene-pentanol, a useful monomer for fluoropolymer synthesis.[18]

Related Reagents. Iodine monochloride; bromine *N*-iodosuccinimide; *N*-bromosuccinimide, *N*-iodosaccharin; iodonium dicollidine perchlorate.

Second Update

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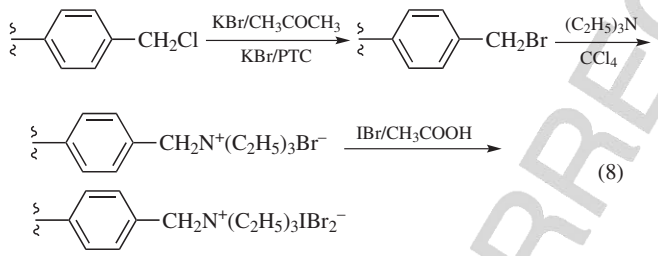
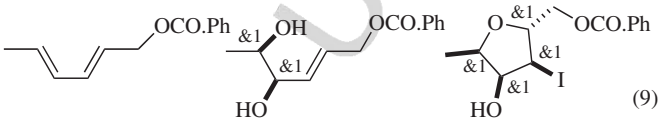
Preparation of Polymeric Polyhalide Reagents. In order to prepare a dibromoiodate resin, the bromomethyl polystyrene, prepared from chloromethyl polystyrene, was quaternized with excess triethylamine to afford polymer-bound benzyltriethylammonium bromide resin. The quaternized resin on reaction with iodine monobromide solution in glacial acetic acid gave the polymer-bound benzyltriethylammonium dibromoiodate reagent (eq 8). The polymeric polyhalide anionic reagents were found to be effective as selective iodinating reagents and are easy to prepare by means of quaternary ammonium salt resins. The bound polyhalide reagents differ from other similar supported reagents in that they possess moderate capacity values. They exhibited effective selectivity toward amines and phenols with a moderate excess of the reagent vs. substrate.[19]



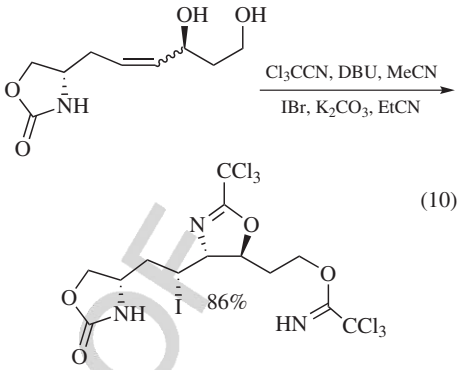
(8)

Electrophilic Cyclization. Using 2 equiv of iodine monobromide resulted in complete cyclization at 10 °C during 16 h. The resulting product was obtained with an enhanced 14:1 ratio in favor of the desired isomer, which was secured in a pure state in 78% yield (eq 9).[20]



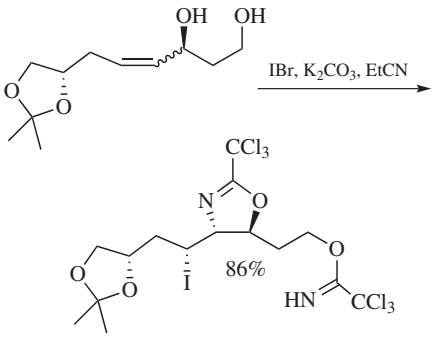
(9)

The purified (Z)-isomer was cyclized with iodine monobromide to give the *trans*-oxazoline in 83% overall yield (eq 10). This compound contains three stereogenic centers of the target alkaloid with the correct absolute configuration.[21]



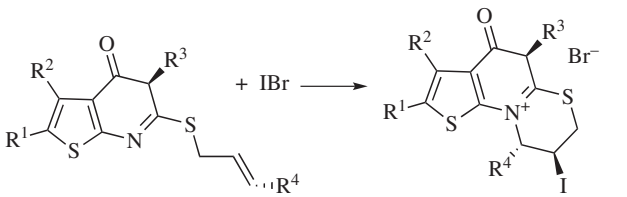
(10)

The bis(trichloroacetimidate) of *cis*-alkene was treated with iodine monobromide to give the *trans*-iodooxazoline as a single stereoisomer in 86% yield (eq 11).[22]



(11)

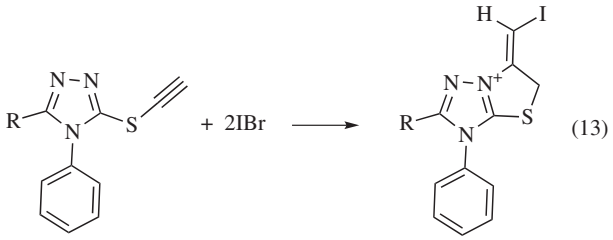
A method of producing salts of 8-halo-4-oxo-2,3,5,9-substituted-5,7,8,9-tetrahydro-4*H*-thieno- [3,2:5,6]-pirymido [2,1-b][1,3] thiazyn-10-ium, which includes electrophilic heterocyclization of terminal propenyl thioethers of thieno[2,3-*b*]pyrimidine under halogen, replaced the starting thioether by 3*N*-pyrimidine (eq 12).[23]



R, R^2 = Alk; R^3, R^4 = Ar

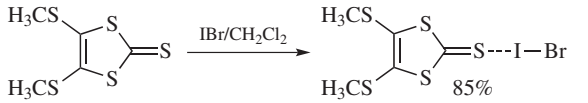
(12)

The cyclization of thioether by iodine monobromide in glacial acetic acid at room temperature leads to formation of condensed compounds with annulation of the thiazoline ring (eq 13).[24]



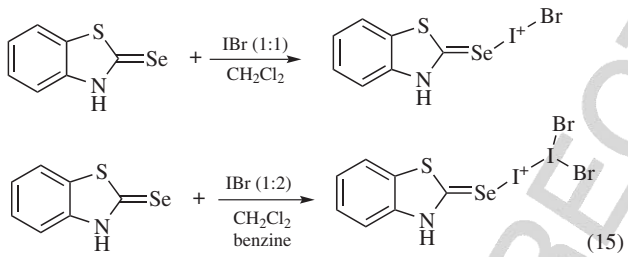
(13)

Electrophilic Addition. Addition of IBr to an equimolar quantity of 1,3-dithiole-2-thione dissolved in refluxing dichloromethane resulted in the formation of an orange-red solution that deposited large brown crystals when cooled to 5 °C overnight (eq 14).[25]



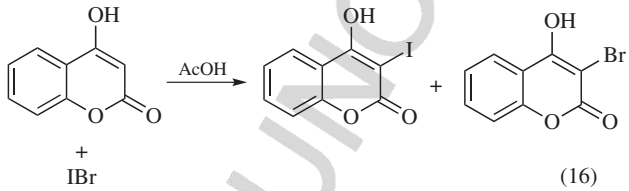
(14)

The reactions of chalcogen donor molecules with halogens and interhalogens can give unpredictable products. Extension of DFT calculations to a larger class of donors and to products obtainable on reaction with IBr is still necessary to elucidate the mechanistic aspects of these reactions (eq 15).[26]



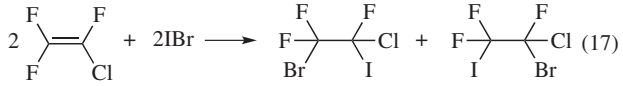
(15)

The iodination of 4-hydroxycouamarin with iodine monobromide led to a mixture of 3-iodo and 3-bromocoumarin (eq 16). Products obtained via the action of visible light on three 3-iodocoumarins in acetone led to the conclusion that the rate of deiodination is dependent on the nature of 4-substituents. Thus, the rate of deiodination for 3-iodo-4-hydroxycoumarin is very fast and gives 4-hydroxycoumarin.[27]



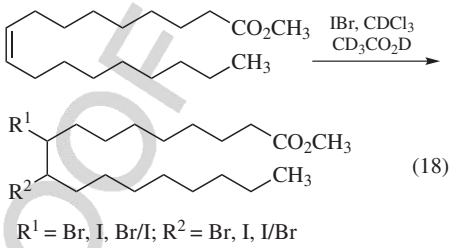
(16)

Electrophilic Addition to Alkenes. The reaction of chlorotrifluoroethylene with iodine bromide has been investigated and a substantial amount of both possible isomers was obtained (eq 17).[28]



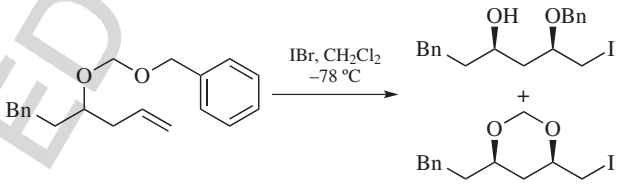
(17)

The reaction of methyl oleate with IBr goes to completion. Since the double bonds in acyl residues of natural fats are isolated, they should react independent of each other, implying a comparable rate of addition of IBr. However, it is found that IBr and these olefins form mixtures of dibromo, bromoiodo, and diiodo alkanes (eq 18).[29]



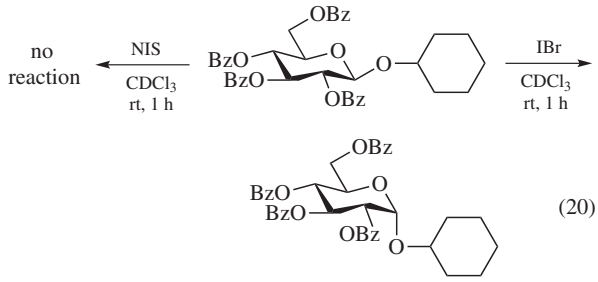
(18)

Intramolecular Oxygen Alkylation. A benzyloxymethyl substrate underwent efficient benzyl ether transfer. Thus, IBr/CH_2Cl_2 provides orthogonally protected *syn*-1,3-diol units via benzyl cleavage, affording the acetal as the major product (eq 19).[30]



(19)

Anomerization. Anomerization was observed from bromide, cyclohexanol, and Ag_2O. No reaction occurred when the acetal was exposed to 2 equiv of NIS for 20 h, while complete anomerization was observed upon reaction with IBr for 1 h (eq 20).[31]



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Author Query

Q1 Please check the author name “Slivka, mar. v.” in ref.[23]. For carrectness.