Bromine Reagents

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Hypervalent Bromine Compounds: Smaller, More Reactive Analogues of Hypervalent Iodine Compounds

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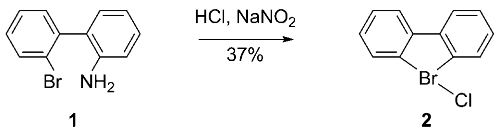
alkyne coupling · hypervalent bromine compounds · hypervalent iodine compounds · Michael addition · oxidation

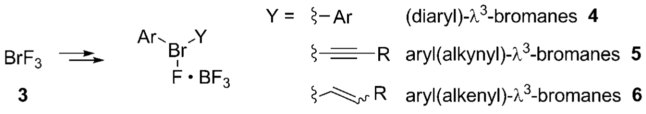
Hypervalent iodine compounds have enjoyed a very rich chemistry in recent years. Many novel reactions have been developed, and new reagents as well as strategies have expanded the repertoire of the synthetic chemist.[1] Hypervalent bromine compounds, however, have not been considered seriously although they have been known for a long time. Already in 1952 the formation of the diazonium salt from amine **1** and subsequent thermal decomposition yielding the λ^3-bromane derivative **2** was described (Scheme 1).[2]



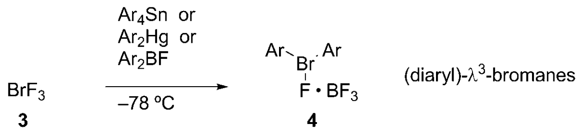
Scheme 1. Synthesis of the first hypervalent bromine derivative **2**.

This synthesis seems to be straightforward, but the intermolecular addition of aryl cations to aryl bromides, irrespective of their precursors and methods of generation, led to only negligible yields of hypervalent bromine compounds.[3] The only useful synthesis of hypervalent bromine compounds to date involves ligand-exchange reactions of bromine trifluoride (**3**).[4] Hypervalent bromine derivatives with the general structures **4**–**6** (Scheme 2) have been reported.[5]

The ligand exchange proceeds, as in λ^3-iodanes,[6] by a low-energy and hence rapid addition–elimination process. Reaction of bromine trifluoride (**3**), a highly toxic and extremely reactive liquid, with arylstannanes, arylmercury, or arylboron compounds leads readily to (diaryl)-λ^3-bromanes of type **4** at low reaction temperatures (Scheme 3). These reactions proceed under Lewis acid catalysis and form a boron trifluoride stabilized product. The λ^3-bromanes **4** are more reactive than their iodine counterparts and react similarly, but faster and at lower reaction temperatures with oxygen, sulfur, and carbon nucleophiles.



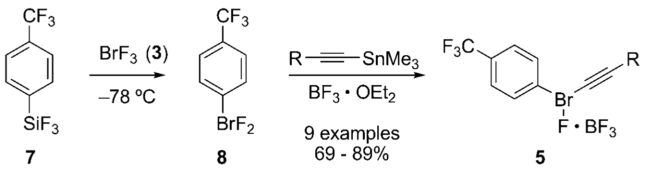
Scheme 2. Different types of hypervalent bromine compounds.



Scheme 3. Synthesis of (diaryl)-λ^3-bromanes **4**.

Not only different reactivities, but completely different reactions have been observed with aryl(alkynyl)-λ^3-bromanes **5** compared to the reactions of hypervalent iodine reagents. Because of the greater electronegativity and the greater ionization potential of the λ^3-bromanes, they are even more powerful Michael acceptors than λ^3-iodanes. The synthesis of aryl(alkynyl)-λ^3-bromanes **5** proceeds easily from arylbromine difluoride **8** by boron trifluoride catalyzed ligand exchange with alkynylstannanes (Scheme 4).[7] Compound **8** can be obtained by reaction of bromine trifluoride (**3**) with the trifluorosilyl derivative **7** in a fluorine–aryl substitution at low reaction temperature as described by Frohn and Giesen.[8]

Compounds **5** can be used in reactions that are completely different from those of the analogous, thoroughly investigated aryl(alkynyl)-λ^3-iodanes. Some of these reactions are shown in Scheme 5. Reactions with tosylate lead to the formation of



Scheme 4. Synthesis of *p*-trifluoromethylphenyl(alkynyl)-λ^3-bromanes **5**.

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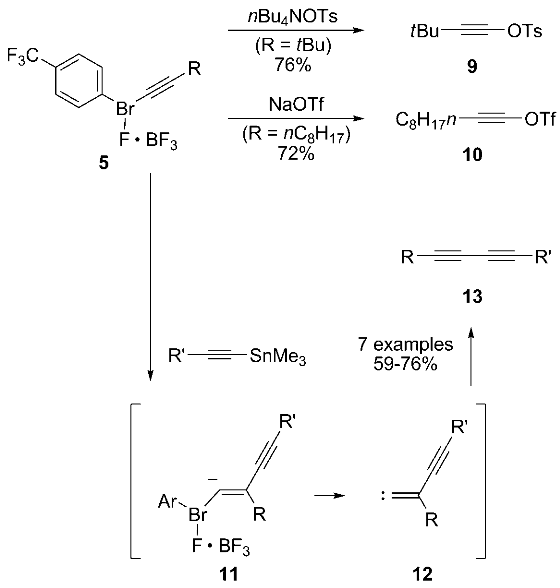
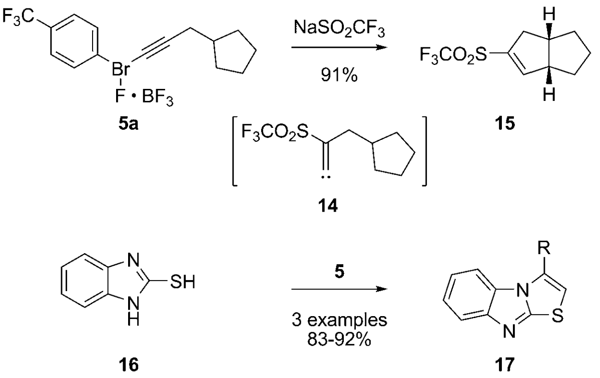


Scheme 5. Alkyne coupling reactions of aryl(alkynyl)-λ³-bromanes **5**.

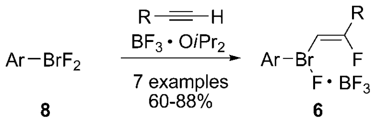
alkynyltosylates **9**. Even triflates can be used to access previously unknown alkynyltriflates **10**.[5] Ochiai, Frohn, and co-workers found that also alkynylstannanes can react in uncatalyzed reactions with **5** to produce diynes **13**—a reaction exclusive to λ³-bromanes. This reaction proceeds by an initial Michael addition of the alkynylstannane to give **11** and a subsequent reductive elimination of the bromine moiety to yield an alkylidene carbene intermediate **12**. This undergoes an 1,2-migration to yield compounds **13**, as analysis of the side products has shown.[9] As the synthesis of **5** and the reaction to **13** both involve alkynylstannanes, the homocoupling of alkynylstannanes can be achieved using arylbromine difluoride **8** with boron trifluoride catalysis.

Various sulfur nucleophiles also react with **5**. This is shown in two selected examples: **5a** reacts with sodium trifluoromethylsulfinate to form the bicyclic sulfone **15** (Scheme 6, top). After the addition of sulfinate to the triple bond and formation of carbene **14**, the reaction is terminated by CH insertion to yield the bicyclic compound **15**.[10] If 2-thiobenzimidazole (**16**) is employed as nucleophile, tricyclic azapentalenes **17** are formed in good yields (Scheme 6, bottom).[11]



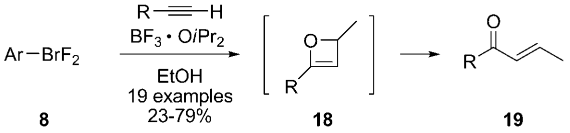
Scheme 6. Reactions of aryl(alkynyl)-λ³-bromanes **5** with sulfur nucleophiles.

The first vinyl bromanes were prepared by reacting vinyl bromide with a fluoromethane–antimony pentafluoride complex.[12] Compounds of type **6** are much more easily accessible by reactions of arylbromine difluoride **8** with terminal alkynes.[13] This reaction generates the stable β-fluoroalkenyl-λ³-bromanes **6** in a highly stereoselective anti-Markovnikoff addition. The reaction conditions were optimized and the best Lewis acid chosen to avoid side products. As shown in Scheme 7 compounds **6** were obtained in good yields.



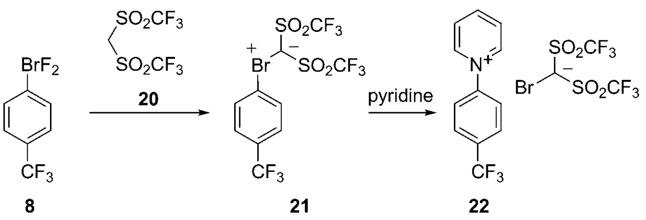
Scheme 7. Synthesis of aryl(alkenyl)-λ³-bromanes **6**.

When a terminal alkyne was treated with **6** in the presence of ethanol, the α,β-unsaturated carbonyl compound **19** was obtained as the only product (Scheme 8).[14] Further investigation of this reaction revealed that the arylbromine difluoride **8** acts as a selective oxidant to generate acetaldehyde. Subsequent Lewis acid catalyzed [2+2] cycloaddition of acetaldehyde and the alkyne leads to the formation of 2*H*-oxete **18**, which opens to form **19** selectively. With the corresponding aryliodine difluoride this reaction is not possible at all.



Scheme 8. Formation of α,β-unsaturated carbonyl compounds **19** from alkynes and arylbromine difluoride in the presence of ethanol.

In analogy to the iodonium ylides, the corresponding bromonium ylides can be prepared from arylbromine difluoride **8** and bis(trifluoromethylsulfonyl)methane (**20**; Scheme 9). Ylide **21** is stabilized by the two strongly electron-withdrawing trifluoromethylsulfonyl groups; its reactivity is different from that of the known iodonium ylides, which undergo transylidation with nucleophiles. Ylide **21**, however, reacts with nitrogen heterocycles under arylation, as the reaction with pyridine to yield **22** demonstrates.[15]



Scheme 9. Synthesis of bromonium ylide **21** and arylation of pyridine.

Reactions with alkenes lead to cyclopropanes, although the yields are higher with the corresponding, even more reactive chloronium ylides.[16]

Very interesting reactivities and reactions of different λ^3-bromanes have already been discovered, and there are surely many more to come. The speed of their discovery will, however, depend on the accessibility of λ^3-bromanes. Until a more suitable precursor than bromine trifluoride (**3**) is found, detailed investigations can be made only by those research groups able to safely handle this starting material.

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