

SYNLETT Spotlight 125

Boron Tribromide

Compiled by Elisa García Doyagüez



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Elisa García Doyagüez studied Chemistry at the Universidad Autónoma de Madrid (2001–2004). She is currently working towards her PhD in Medicinal Chemistry under the supervision of Dr. M. I. Rodríguez-Franco at the Instituto de Química Médica of Consejo Superior de Investigaciones Científicas (CSIC) of Spain. Her research includes the synthesis of antioxidant polyphenols and related structures using boron tribromide.

Instituto de Química Médica (CSIC), Juan de la Cierva, 3, 28006 Madrid, Spain
E-mail: elisagdoyaguez@iqm.csic.es

Introduction

Boron halides are useful reagents in organic chemistry. Among them, boron tribromide must be highlighted, due to the different reactions that it can perform, such as cleavage of ethers, amines, and thiols, and addition to alkenes and alkynes. These are many examples of its use in medicinal chemistry,¹ in the synthesis of natural products,² and in the development of new organic materials.³

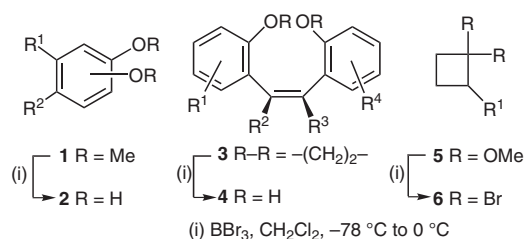
BBr_3 is a colourless fuming liquid. It is commercially available neat, or in solution with dichloromethane or hexanes.

Precautions: BBr_3 is highly moisture-sensitive and decomposes in air with evolution of HBr . It must be stored under a dry inert atmosphere. It reacts violently with protic solvents such as water and alcohols; ethers are also inappropriate solvents.

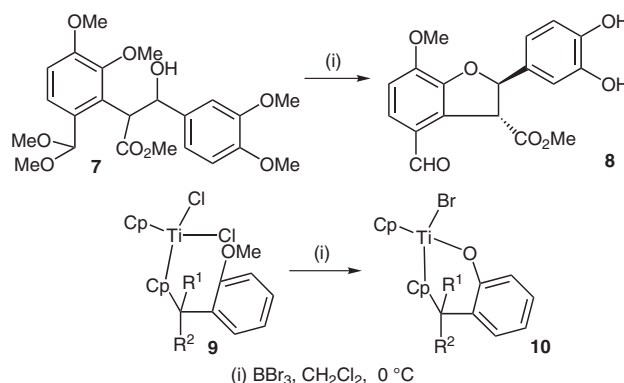
Abstracts

(A) *Cleavage of ethers.* Boron-based reagents are particularly versatile for cleaving C–O bonds, giving an alkyl bromide and an alkoxyborane that then is hydrolyzed to the corresponding alcohol. Alkyl aryl ethers are cleaved at the alkyl–oxygen bond, yielding the corresponding phenol and the alkyl bromide. However, the cleavage of mixed dialkyl ethers usually takes place at the more substituted carbon–oxygen bond, giving secondary or tertiary alkyl bromides.

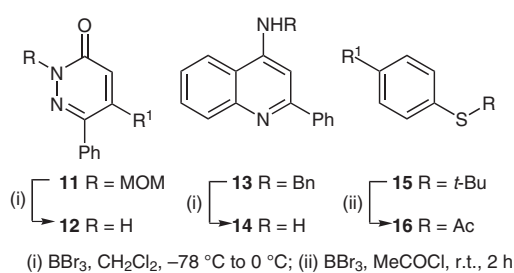
In the cleavage of aryl methyl ethers, boron tribromide is more effective than other reagents like iodotrimethylsilane.⁴ When several alkoxy groups were present on the aromatic ring (**1**), treatment with BBr_3 led to the deprotection of all of them in high yields (**2**).⁵ Mayekar et al. removed the dimethylene spacer group from cyclic stilbenes **3** to obtain the geometrically pure acyclic stilbene isomer **4** in good yield, without isomerization of the stilbene double bond.⁶ Recently, Nordvik and Brinker described a novel route to geminal dibromocyclobutanes **6** that involved the treatment of the corresponding cyclobutanone acetal **5** with BBr_3 .⁷



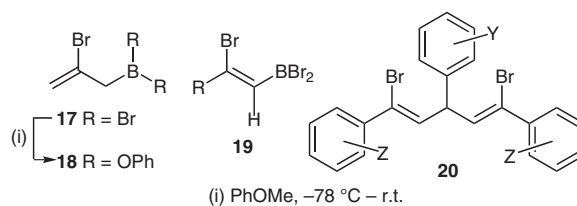
(B) *Cleavage of ethers and cyclization.* These tandem transformations involve the deprotection of an ether and the consequent intramolecular cyclization. This strategy has been used for the fully diastereoselective cyclization of different precursor molecules like **7**, obtained by an aldol-type reaction, to a series of hydroxylated aryldihydrobenzofurans **8**, that are often key structures in natural products.⁸ Qian et al. studied the intramolecular cyclisation of cyclopentadienyl titanium complexes **9** to form titanoxacycle complexes **10** promoted by BBr_3 . A probable two-step mechanism involving halogen exchange and intramolecular elimination was proposed.⁹



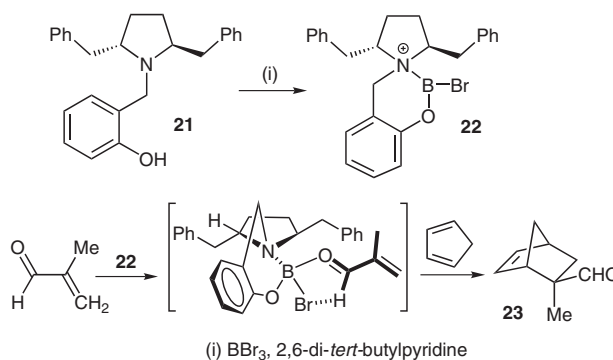
(C) *Cleavage of amines and thiols.* Since BBr_3 can also cleave C–N and C–S bonds under mild reaction conditions, it has been used for the removal of both amino and thiol protecting groups. Sotelo et al. presented a selective procedure for the cleavage of a methoxymethyl group at the 2-position of acid-sensitive pyridazinones **11** without affecting the double bonds in the molecule.¹⁰ Paliakov and Strekowski reported that the treatment of benzylamino quinolines **13** with BBr_3 yielded the corresponding amino derivative **14** in high yield, using short reaction times.¹¹ Recently, the *tert*-butyl moiety, a base-resistant thiol protecting group, was smoothly replaced by the labile acetyl moiety in one pot (**15** \rightarrow **16**), using a mixture of BBr_3 and acetyl chloride.¹² This strategy has been used in the synthesis of oligo(phenylenevinylene)s (OPVs), new organic materials with electrical and optical properties.¹³



(D) *Addition to allenes and alkynes.* BBr_3 reacts easily with allenes and alkynes to give bromoboration products. Thus, reaction of BBr_3 with allene at -20°C gives (2-bromoallyl)dibromoborane **17**, that then can react with anisole to yield (2-bromoallyl)diphenoxyborane **18**.¹⁴ Reactions of BBr_3 with alkynes usually occur in a stereo-, regio-, and chemoselective manner via the *syn* addition of the B–Br moiety to the $\text{C}\equiv\text{C}$ bond, generating the corresponding (*Z*)-(2-bromo-1-alkenyl)dibromoborane **19**. These vinylboranes are versatile intermediates that can be used in transformations such as additions to carbonyl compounds. A recent example is the reaction of aryl aldehydes with two equivalents of arylacetylenes in the presence of BBr_3 ; this generated the pure isomer (*Z,Z*)-1,3,5-triaryl-1,5-dibromo-1,4-pentadiene **20**.¹⁵



(E) *Chiral borane reagents.* The use of chiral Lewis acids as catalysts for asymmetric Diels–Alder reactions has transformed the classical thermal cycloaddition, one of the most versatile and useful processes in synthetic chemistry. Complexes made from chiral pyrrolidines and BBr_3 are effective catalysts for these cycloadditions. Sprott and Corey recently described that the treatment of 2,5-dibenzylpyrrolidine **21** with 2,6-di-*tert*-butylpyridine and BBr_3 led to the formation of **22**, which catalyzes the Diels–Alder reaction of cyclopentadiene and 2-methylacrolein to form the *exo* adduct **23** in 96% yield and 96% ee.¹⁶



References

- (1) Lisowski, V.; Léonce, S.; Kraus-Berthier, L.; Sopková de Oliveira Santos, J.; Pierré, A.; Atassi, G.; Caignard, D.; Renard, P.; Rault, S. *J. Med. Chem.* **2004**, *47*, 1448.
- (2) Brimble, M. A.; Brenstrum, T. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1624.
- (3) Vlachos, P.; Kelly, S. M.; Mansoor, B.; O'Neill, M. *Chem. Commun.* **2002**, 874.
- (4) Vickery, E. H.; Pahler, L. F.; Eisenbraun, E. J. *J. Org. Chem.* **1979**, *44*, 1979.
- (5) Barluenga, J.; Aznar, F.; Palomero, M. A. *J. Org. Chem.* **2003**, *68*, 537.
- (6) Mayekar, N. V.; Chattopadhyay, S.; Nayak, S. K. *Synthesis* **2003**, 2041.
- (7) Nordvik, T.; Brinker, U. H. *J. Org. Chem.* **2003**, *68*, 9394.
- (8) Detterbeck, R.; Hesse, M. *Helv. Chim. Acta* **2003**, *86*, 343.
- (9) Qian, Y.; Huang, J.; Ding, K.; Zhang, Y.; Huang, Q.; Chen, X. P.; Chan, A. S. C.; Wong, W. T. *J. Organomet. Chem.* **2002**, *645*, 59.
- (10) Sotelo, E.; Coelho, A.; Raviña, E. *Tetrahedron Lett.* **2001**, *42*, 8633.
- (11) Paliakov, E.; Strekowski, L. *Tetrahedron Lett.* **2004**, *45*, 4093.
- (12) Stühr-Hansen, N. *Synth. Commun.* **2003**, *33*, 641.
- (13) Stühr-Hansen, N.; Christensen, J. B.; Harrit, N.; Bjørnholm, T. *J. Org. Chem.* **2003**, *68*, 1275.
- (14) Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1991**, *32*, 6749.
- (15) Kabalka, G. W.; Wu, Z.; Ju, Y. *Org. Lett.* **2002**, *4*, 1491.
- (16) Sprott, K. T.; Corey, E. J. *Org. Lett.* **2003**, *5*, 2465.