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Thermal and microwave hydrolysis of organotrifluoroborates mediated by alumina

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ABSTRACT

Hydrolysis of organotrifluoroborates to the corresponding organoboronic acids is readily achieved under either thermal or microwave conditions in the presence of alumina. The organoboronic acid products are obtained in good to excellent yields with essentially no loss of boronated reagent due to protoboronation.

Organoboronic acids have become fundamental building blocks in synthetic organic chemistry with the advent of the Suzuki Miyaura coupling reaction.[1] The fact that ester derivatives and trifluoroborate salts also undergo a wide variety of metal-catalyzed coupling reactions has only served to enhance the importance of the organoboronic acids.[2] The facile conversion of organoboronic acids to trifluoroborate and ester derivatives has permitted researchers to utilize whichever organoboron derivative that reacts most effectively.[3] However, the hydrolysis of organotrifluoborates to the corresponding organoboronic acids can be problematic.[4]

We have had a continued interest in organic reactions carried out in the presence of alumina.[5] We have also been interested in the use of microwave irradiation for enhancing organic reactions[6] including those involving organotrifluoroborate reagents.[7] Because of these interests, we investigated the potential use of microwave irradiation in the hydrolysis of organotrifluoroborate derivatives. Since earlier studies made it clear that the hydrolysis reaction proceeds more rapidly in the presence of a base, we initiated the studies under basic conditions.[4] We found that that the hydrolysis of organotrifluoroborates proceeds far more rapidly upon microwave irradiation than under thermal conditions (reaction times decrease from 24 h to a matter of minutes). As was noted in the earlier reports, aromatic trifluoroborates containing electron-donating groups hydrolyze more rapidly that those containing electron-withdrawing groups under either thermal or microwave conditions.

In our hands, bases such as Na_2CO_3 and $NaHCO_3$ were effective for hydrolyzing aryltrifluoroborates containing electron-donating groups in the microwave reactions.[8] However, we found that hydrolysis products from aryltrifluoroborates derivatives containing electron-withdrawing groups often contained significant amounts of the protonolysis byproducts. Protonolysis also occurred when an organic base such as Hunig's base was utilized in the microwave-induced hydrolysis reactions. It should be noted that hydrolysis reactions of the organotrifluoroborates can be readily monitored by thin layer chromatography and product purity analyzed by boron-11 and hydrogen-1 NMR (the organotrifluoroborates exhibit resonances near 7 ppm, boric acid resonates near 20 ppm, and the organoboronic acids resonate near 30 ppm.)

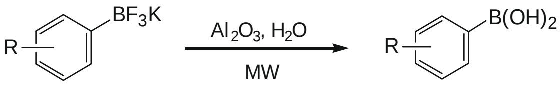
We then examined the hydrolysis reactions in the presence of alumina using microwave irradiation carried out in a commercial monomode reactor, Scheme 1.

The hydrolysis reaction proceeded rapidly and in a very high yield for all aryltrifluoroborates investigated. Significantly, no trifluoroborate starting material remained after hydrolysis and protonolysis was not observed for any of the materials examined, Table 1. The reactions were quite straightforward in that the product arylboronic acids were recovered by simple extraction (ethyl acetate) followed by evaporation of the solvent. (NMR can be used to monitor product purity.)

We then examined the reaction under thermal conditions. At ambient temperatures, the hydrolysis reactions proceeded at a relatively low rate (reaction times ranged from 12 to 24 h. However, hydrolysis proceeded quite readily at 70 °C. The synthetic procedure parallels that used in the microwave reactions, Scheme 2.[10]

We also examined the hydrolysis of a vinyltrifluoroborate and an alkyltrifluroroborate derivate, Scheme 3. The reactions proceeded in excellent yields with no evidence of protonolysis. In each case, the isolated yield of pure products was excellent, Scheme 3.

Although a detailed mechanistic study has not been carried out, the efficacy of alumina in the hydrolysis reactions may be due in part to the large enthalpy of the aluminum fluoride bond and the fact that the resultant product is insoluble in the reaction mixture.



Scheme 1. Hydrolysis of organotrifluoroborates.

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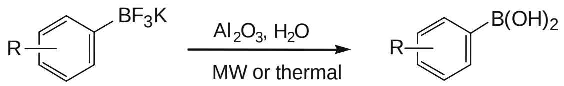
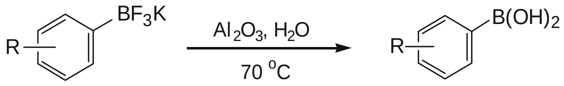
Table 1
Hydrolysis of organotrifluoroborates

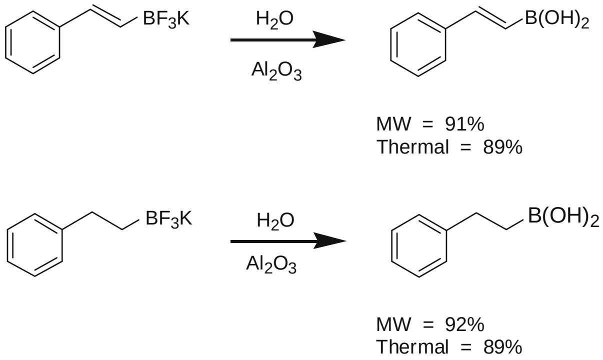


Entry	R	MW Yield[a] (%)	Thermal yield[a] (%)
1	4-CH_3	90	88
2	4-F	94	90
3	4-OCH_3	93	92
4	2-OCH_3, 5-OCH_3	87	84
5	4-CHO	92	89
6	4-CH_3CO	95	91
7	4-CF_3	85	82

[a] Isolated yields of pure products. Reactions were carried out at 70 °C for 15 min. See Refs. 9 and 10 for experimental details.



Scheme 2. Hydrolysis under thermal conditions.



Scheme 3. Hydrolysis of an alkenyl- and alkyl-trifluoroborates.

A parallel hypothesis has been put forth to explain the efficiency of lithium hydroxide in hydrolysis reactions of organotrifluoroborates under solution conditions.[4a]

In conclusion, we have developed a straightforward procedure for hydrolyzing organotrifluoroborates to the corresponding boronic acids in excellent yields under very mild conditions.[11] In contrast to previously reported organotrifluoroborate hydrolysis reactions, protodeboronation is not observed.

Acknowledgments

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8. Interestingly, LiOH was ineffective for hydrolyzing organotrifluoroborates under our reaction conditions.
9. Representative procedure: to a solution of potassium 4-formylphenyltrifluoroborate (212 mg, 1.00 mmol) in 10 mL of water was added 0.2 g of Al_2O_3 contained in a 25 mL round-bottomed flask. The resulting suspension was inserted into a CEM Discover microwave unit and stirred for 15 min at 70 °C. The mixture was extracted with ethyl acetate (3 × 10 mL), the extracts combined, dried over anhydrous sodium sulfate, filtered, and the solvent evaporated to yield 4-formylphenylboronic acid as a white solid (134 mg, 92%).
10. The procedure paralleled that described in Ref. 9 except that the stirred mixture was heated in an oil bath at 70 °C for a period of 30 min.
11. During the review process, we were made aware of a new hydrolysis procedure developed by Molander and his group {*Journal of Organic Chemistry*, ASAP}.