Preparation and Reactions of Mesityleneboronic Acid

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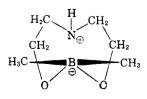
Although many aryl boronic acids and esters have been described in the chemical literature, no reference has been found to a 2,6-di-substituted phenylboronic acid. Such a material was of interest for the purpose of exploring the steric effect of 2,6 substituents upon the chemical properties of the boronic acid group. We therefore chose to prepare mesitylene boronic acid and to study its behavior in a series of common reactions.

Mesityleneboronic acid was prepared in 28%yield by the reaction of methyl borate with the mesityl Grignard reagent. The resulting boronic acid was purified by recrystallization from benzene and fully characterized. It melted sharply at 143– 145° followed by resolidification and a second melting point was observed in the neighborhood of 190°. Examination of the material melting at 190° proved it to be the anhydride of mesitylene boronic acid.

Mesityleneboronic acid was smoothly converted to its *n*-butyl ester by treatment with *n*-butyl alcohol in boiling toluene. This ester was easily reconverted to mesityleneboronic acid by brief treatment with dilute sodium hydroxide solution. The lithium aluminum hydride reduction of di-*n*-butyl mesitylene boronate in ethyl ether and in the presence of pyridine at -80° afforded pyridine mesitylene borane in 78% yield. This material was normal in all respects in that it gave rapid reduction of iodine to iodide ion, silver ion to silver metal, and evolved hydrogen on treatment with dilute hydrochloric acid.

Since diethanolamine had been previously shown by Letsinger and Skoog¹ to afford air stable and crystalline derivatives with aryl boronic acids, several attempts were made to prepare the diethanolamine ester of mesityleneboronic acid. In each case no stable diethanol amine ester was obtained. This result is attributed to the steric inability of the diethanolamine nitrogen atom to readily coordinate with the boron atom of the diethanolamine ester to produce a tetrahedral boron atom.

Treatment of mesityleneboronic acid with hot



(1) R. L. Letsinger and I. Skoog, J. Am. Chem. Soc., 77, 2491 (1955).

NOTES

As the above results show, mesityleneboronic acid is apparently as reactive as phenyl boronic acid and similar aryl boronic acids toward anhydride formation, esterification, and reduction to the pyridine borane derivative. Only in the case of the diethanolamine ester is the steric effect of 2,6dimethyl substitution apparent. Since there is little doubt that a steric effect does exist in reactions of mesitylene boronic acid which proceed through a transition state containing a tetrahedral boron atom, it must be concluded that such reactions of aryl boronic acids and derivatives are so rapid in general that this steric retardation goes unnoticed by the qualitative observer. This is in contrast to the observations made with mesitoic acid and its esters.

EXPERIMENTAL

Preparation of mesityleneboronic acid. To a suspension of 5 g. of magnesium and a crystal of iodine in 20 ml. of ether was slowly added 40 g. (0.20 mole) of 2-bromomesitylene dissolved in 200 ml, of dry ether. This addition was carried out under nitrogen and over a 4-hr. period. The resulting mesitylmagnesium bromide was added dropwise with vigorous stirring to 21 g. of methyl borate dissolved in 200 ml. of dry ether at -78° . After the addition, the reaction mixture was allowed to warm to room temperature and to remain at that temperature overnight. The Grignard complex was decomposed by the slow addition of 200 ml. of 4N hydrochloric acid at 0°. The ether layer was separated, washed well with water, and dried over magnesium sulfate. Removal of the solvent under vacuum afforded an oil which was treated with two volumes of pentane. On standing the oil crystallized and 9.1 g. (28% of theory) of mesitylene boronic acid was collected by filtration. Recrystallization from benzene afforded 5.5 g. of material melting at 143-145°. Continued heating resulted in resolidification of the melt followed by the observation of a second m.p. at 193–197°

Anal. Calcd. for $C_{9}H_{13}BO_{2}$. C, 65.90; H, 7.99; B, 6.60. Found. C, 66.27; H, 8.22; B, 6.50.

Preparation of mesitylene boronic acid anhydride. One g. of mesityleneboronic acid was placed in a test tube and immersed in an oil bath maintained at 150°. The boronic acid rapidly melted and water vapor was seen to condense on the upper portion of the tube. Continued heating resulted in the resolidification of the melt and all residual water was removed by the application of vacuum. The resulting mesityleneboronic acid anhydride melted at 205-210° and showed no absorption in the hydroxyl region of the infrared.

Anal. Caled. for C₉H₁₁BO: C, 74.04; H, 7.59. Found: C, 73.77; H, 7.61.

The anhydride was also prepared by azeotropic distillation of mesityleneboronic acid with benzene. After 8 hr. the theoretical amount of water had been collected and anhydride melting sharply at 209-210° separated from the benzene solution on cooling.

Di-n-butyl mesityleneboronate. In a Stark-Dean apparatus were heated overnight 5.5 g. of mesityleneboronic acid (0.034 mole) 50 ml. of benzene and 50 ml. of *n*-butyl alcohol. The major portion of the solvent was removed by distillation and the residual oil vacuum distilled to give 5.5 g. (59%) of ester boiling at $122-124^{\circ}$ at 3 mm.

Anal. Calcd. for C₁₇H₂₉BO₂: C, 73.92; H, 10.58. Found: C, 73.80; H, 10.21.

Attempted preparation of the diethanolamine ester of mesityleneboronic acid. To 100 ml. of toluene was added 4.1 g. $(2.5 \times 10^{-2} \text{ mole})$ of mesityleneboronic acid and 2.6 g. $(2.5 \times 10^{-2} \text{ mole})$ of diethanolamine. The resulting mixture was refluxed in a Stark-Dean apparatus for 3 hr. after which time water was no longer evolved. The toluene solution was cooled and treated with 100 ml. of pentane. Upon the addition of pentane an oily phase separated which would not crystallize upon repeated cooling and scratching of the glass surface. A small portion of the oil was separated and found to be completely miscible with water.

In a similar experiment di-*n*-butyl mesityleneboronate and an equivalent quantity of diethanolamine were placed in a large quantity of toluene and the toluene slowly distilled. After removal of the final traces of solvent in vacuum the residue was dissolved in a small portion of ethanol and crystallization was attempted without success.

Although the diethanolamine ester of mesityleneboronic acid was probably produced in both of the experiments described above the isolation of this compound by the methods chosen was perhaps unsuccessful due to its innate instability. Normally diethanolamine esters of aryl boronic acids are easily crystallized high melting solids which allow easy isolation.

Preparation of pyridine mesityl borane. Lithium aluminum hydride (0.8 g.) was refluxed with 50 ml. of ether for 1 hr. in a nitrogen atmosphere. The solution was cooled to -80° and 3 ml. of dry pyridine added. This solution was vigorously stirred under nitrogen as 5.2 g. (0.019 mole) of di-*n*-butyl mesityleneboronate dissolved in 15 ml. of ether was added dropwise at -80° over 1-hr. period. Following the addition the reaction mixture was allowed to stir at -80° for 0.5 hr. and was then warmed to 0°. At 0° 2 ml. of pyridine dissolved in 4 ml. of water was added. The solution was filtered and the solvent removed in vacuum. The crystalline solid residue was recrystallized from ether pentane to afford 3.1 g. (78% theory) of pyridine mesityl borane melting at 116–118°.

Anal. Calcd. for $C_{14}H_{18}BN$: C, 79.64; H, 8.59; B, 5.13. Found: C, 79.74; H, 8.74; B, 5.09.

The acid catalyzed cleavage of mesityleneboronic acid. Mesityleneboronic acid (1.0 g.) was refluxed with 20 ml. of 10% sulfuric acid for 2 hr. Mesitylene was observed in the reflux condenser immediately after mixing the reagents. The reaction mixture was cooled and extracted with pentane. The pentane extract was washed once with water, dried over magnesium sulfate, and the solvent removed in vacuum. The residual oil weighed 0.6 g. and was identified as mesitylene by its infrared spectrum.

Hydrolysis of di-n-butyl mesityleneboronate. Two grams (0.0073 mole) of di-n-butyl mesityleneboronate was stirred magnetically at room temperature with 20 ml. of 10% sodium hydroxide solution. After a reaction period of 0.5 hr. the mixture was extracted with ethyl ether and the aqueous layer acidified with dilute hydrochloric acid. Whereupon, 1.05 g. (88%) of mesityleneboronic acid m.p. $140-145^{\circ}$ was obtained.

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A Convenient Method for Synthesizing Normal Aliphatic 2,4-Dienals

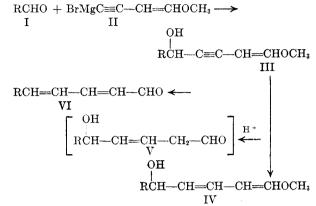
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Recently Marshal and Whiting¹ prepared a number of p-methoxyphenylpolyenealdehydes and

(1) D. Marshal and M. C. Whiting, J. Chem. Soc., 4082 (1956).

one polyene aliphatic aldehyde. Their results suggested that a general preparation of 2,4-dienals can be based on the sequence of reactions shown below. We have found that these reactions proceed



smoothly and that the normal aliphatic 2,4-dienals (VI) are readily obtained.

One might expect the enol vinyl ether (IV), on treatment with acid, to give the aldehyde (V). However, during this step there is spontaneous dehydration and rearrangement of the double bonds and the 2,4-dienals (VI) are isolated. Similar behavior of certain enol vinyl ethers of type IV has been reported by Inhoffen, Bohlmann, and Rummert² and Marshal and Whiting.¹ If the reaction proceeds through the enolaldehyde (V), some dehydration involving carbon atoms 5 and 6 would probably occur giving rise to some 3,5-dienal. In this study there was no indication that these isomers were formed. Neither did the workers cited above report the formation of 3,5-dienal isomers.

Table I lists the yields and data as determined on freshly distilled normal aliphatic 2,4-dienals. The 8, 10, and 12 carbon aldehydes are reported here for the first time. The aldehydes were obtained as pale yellow-green liquids. About 80% or more of the aldehydes could be recovered on redistillation after several months of storage in the dark at -34° ; hence they were reasonably stable under these conditions. However some change had occurred during this storage as was evident from an observed increase in specific gravity and occasional appearance of solid polymer. On exposure to air at room temperature, the aldehydes underwent a relatively rapid polymerization and developed odors suggestive of the nutty, fatty, stale, or rancid types.

Table II lists data observed for the 2,4-dinitrophenylhydrazones. These derivatives showed a tendency to crystallize in polymorphic forms. Melting points, color, and crystalline forms listed in Table II are for forms most commonly obtained. The analytical data and the ultraviolet spectral properties confirm that these are derivatives of 2,4-

⁽²⁾ H. H. Inhoffen, F. Bohlmann, and G. Rummert, Ann., 569, 226 (1950).