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FORMATION AND USE OF BORON SULFONATES

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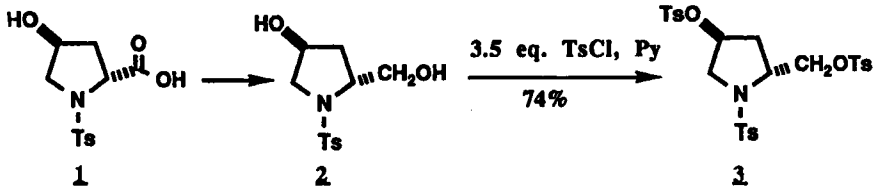
'RACT: Boric acid reacts swiftly with p-toluenesulfonyl chloride idine-d_5 to form the unstable boron sulfonate which is observed IR. The utility of this reaction is discussed.

luction: In a previous communication from this laboratory[1], we ed the synthesis of (*R,R*)-2-methyl-2,5-diazabicyclo[2.2.1] ne from allo-4-hydroxy-D-proline. During the synthesis we ved that the formation of the tritosyl intermediate **3** from the diol ays required more than the theoretical two equivalents of p-esulfonyl chloride for the reaction to proceed to completion. ıl analysis of this reaction has led to a useful procedure for the al of excess p-toluenesulfonyl chloride from reaction mixtures.



Discussion: Initially we thought the excess p-toluenesulfonyl chloride was required due to the steric hindrance of the secondary alcohol. However, it was found that the p-toluenesulfonyl chloride was all consumed at the end of the reaction. The water content of the reaction was found to be less than 0.2% by Karl Fisher titration and therefore the excess p-toluenesulfonyl chloride was not being consumed by water. On the other hand samples of intermediate 3 that have been purified by chromatography, only required the theoretical amount (2 eq.) of p-toluenesulfonyl chloride[2]. At this point we hypothesized that the crude diol 2 probably contained some boron residues from the previous step, which is the reduction of the acid 1 with sodium borohydride in the presence of borontrifluoride•etherate. This would imply that these boronate esters are responsible for the consumption of the p-toluenesulfonyl chloride. To test this hypothesis, a sample of p-toluenesulfonyl chloride and boric acid[3] was mixed in pyridine; this resulted in an exothermic reaction which required external cooling. TLC analysis of the reaction at this point showed no p-toluenesulfonyl chloride and only p-toluenesulfonic acid was recovered. To study this interaction further samples of p-toluenesulfonyl chloride and boric acid were mixed in pyridine-d_5 and

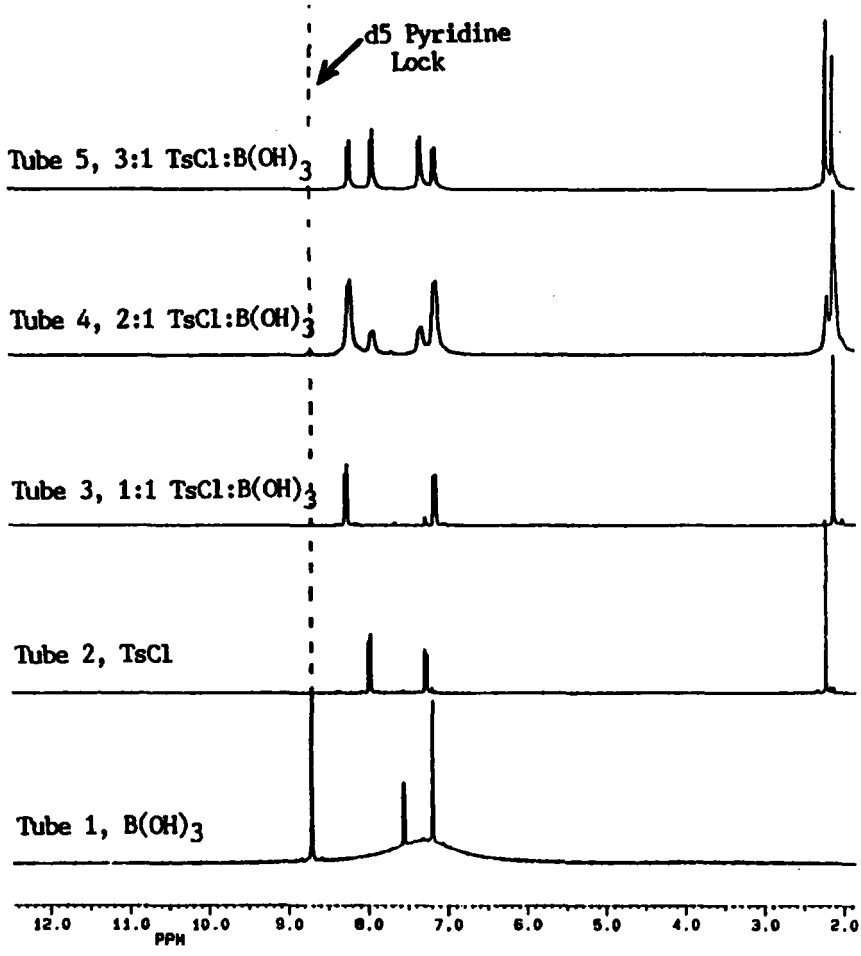
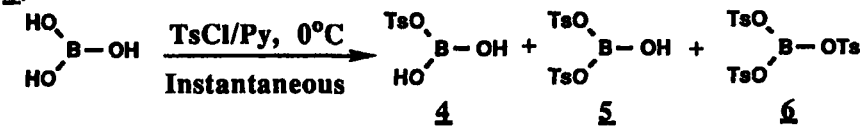


FIGURE 1

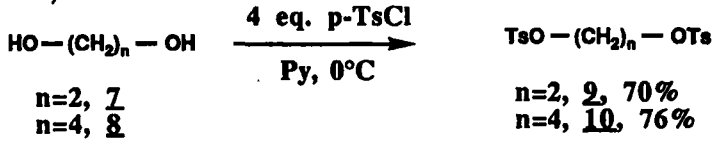
observed by NMR[4]. Sample 1 contained only boric acid and sample 2 contained only p-toluenesulfonyl chloride. Samples 3, 4, and 5 contained a 1:1, 1:2 and 1:3 molar ratio of boric acid to p-toluenesulfonyl chloride respectively[5]. The results of this NMR study are presented in figure 1.

It is apparent from these NMR spectra that a boron tosylate species has formed and the stoichiometry suggests that this species is actually **4**.



4 **5** **6**

The utility of this reaction becomes apparent in situations where excess p-toluenesulfonyl chloride is required for a reaction to proceed to completion and removal of the excess sulfonyl chloride becomes necessary at the end of the reaction. One such case is in the synthesis of the useful[6] 1,4-butanediol bis(4-toluylsulfonate)[7] **10** from 1,4-butanediol, where formation of tetrahydro furan is a byproduct. In this case excess p-toluenesulfonyl chloride (4 eq.) is used at 0°C and this excess was hydrolyzed by the addition of boric acid at the end of the reaction. 1,2-Ethanediol was treated in the same manner to obtain 1,2-ethanediol bis(4-toluylsulfonate) **9** in 70% yield (M.P.= 123-125°C, Lit.[7] 126°C).



In conclusion, we have shown that boron residues complexed to alcohols react with sulfonylchlorides. These boron sulfonates formed quickly and were observed by NMR. This reactivity was shown to be useful in destroying excess p-toluenesulfonyl chloride in pyridine[8].

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were

recorded on a Brucker 250MHz spectrometer using TMS as an internal standard. All reagents were used as received without any purification.

(2R,4S)-1-(4-Toluenesulfonyl)-2-((4-toluenesulfonyl)oxy)-methyl-4-((4-toluenesulfonyl)oxy)pyrrolidine 3: To an ice-cold solution of (2S, 4R)-2-hydroxymethyl-4-hydroxy-N-(p-toluenesulfonyl)-pyrrolidine (17 g, 62.6 mmol) in 50 ml of pyridine was added 4-toluenesulfonyl chloride (41.8 g, .219 mol) in 3 portions in order to keep the temperature of the reaction below 15°C for 1h and the reaction was then allowed to stir at room temperature for 16h. The mixture was then cooled with an ice bath and boris acid (7 g, 113 mmol) was added. The reaction becomes a thick slurry after 10 min and 30 ml of water was added to keep the mixture stirring. After 30 min. 300 ml of 10% aqueous HCl solution was carefully added. A white precipitate formed which was isolated via filtration and then taken in 100 ml of ethanol and heated to reflux for 30 min. The mixture was then cooled and the solids were filtered and dried under reduced pressure to give 23.4 g g of product in 88% yield. M.P.= 134-135°C. NMR($CDCl_3$): 7.8-7.3 (m, 12H), 4.78 (m, 1H), 4.32 (m, 1H), 4.1 (m, 1H), 3.8 (m, 2H), 2.45 (s, 6H), 2.41 (s, 3H), 2.04 (m, 2H). $[\alpha]_D$ = -56.0° (c=1.168, acetone). Lit. $[\alpha]_D$ = -52.5° (c=1.92, acetone).

1,4-butanediol-bis(4-toluenesulfonate) 10:

1,4-butanediol (3g, 33.3 mmol) was dissolved in 20 ml of pyridine and the mixture was cooled to 0°C before p-toluenesulfonyl chloride (25.4 g, 133.2 mmol) was added in portions over a period of 30 min. After stirring at 0°C for 3h, boric acid (8.2 g, 133.2 mmol) was added. The mixture becomes very thick at this point and 20 ml of water was added.

The mixture was stirred for 30 min at room temperature followed by the normal workup with 10% HCl and extraction with (2X50ml) methylene chloride. The combined organic layers were dried over $MgSO_4$ and evaporated to give 10.1 g of desired product in 76% yield (Lit[7] 40%). This product was recrystallised by dissolving it in minimum amount of ethylacetate and hexane was added to produce white flakes (M.P.=69-71°C, Lit[7] 70°C).

Acknowledgement: The author is grateful to Dr. Earl Whipple for providing the NMR data described in FIGURE 1.

REFERENCES

1 Braish, T.F., Fox, D.E.; J. Org.Chem., 1990, 55, 1684.

2 Samples of 2 were usually crystalized from methanol-water.

3 We are assuming that boric acid will behave in a similar manner to boronate esters.

4 These samples required external water cooling upon mixing since this reaction is exothermic.

5

	$B(OH)_3$	p-TsCl
Tube 1	15.46mg(0.25)*	-
Tube 2	-	47.66mg(0.25)
Tube 3	15.46mg(0.25)	47.66mg(0.25)
Tube 4	15.46mg(0.25)	95.32mg((0.5)
Tube 5‡	15.46mg(0.25)	143mg(0.75)

All samples were run in 0.5 ml of pyridine-d_5. All samples were cooled in an ice bath while being mixed. • Number in parenthesis indicates mmoles. ‡ This sample was heterogeneous.

6 Martin E.M., Bulkowski J.E.; J. Org.Chem., 1982, 47, 415.

7 Ribes F., Guglielmetti R., Metzger J.; Bull.Soc.Chim.Fra., 1972, 144.

8 This procedure is not effective in cases where Schotten-Baumann conditions are used. This is possibly due to the lack of solubility of boric acid in organic solvents such as methylene chloride.

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