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A study on the formation of *N*-tosyl-1,3,2-oxazaborolidin-5-one by electrospray mass spectrometry

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Abstract

The crude product generated in a reaction between *N*-tosyl valine and borane was studied by electrospray mass spectrometry (ESIMS). Intermediates in the formation of *N*-tosyl-1,3,2-oxazaborolidin-5-one **1a** and further reactions of **1a** were studied with negative ion mode. According to the results **1a** may, as soon as it is generated, react with the starting amino acid.

1. Introduction

Chiral *N*-sulphonylated 1,3,2-oxazaborolidin-5-ones are known as efficient catalysts/promoters for asymmetric Diels–Alder,[1] Mukaiyama aldol,[2–4] and 1,3-dipolar cycloaddition[5] reactions of nitrones with ketene acetals. Oxazaborolidinones are prepared by allowing borane[6] or boronic acid[7] to react with the corresponding amino acid. Oxazaborolidines, being efficient Lewis acids will react as soon as produced to form adducts with the Lewis basic precursors (e.g. boronic acid or amino acid) present in the solution. We recently described[8] a mass spectrometric study on the formation of *N*-tosyl-2-phenyl-1,3,2-oxazaborolidin-5-one **1b** (Scheme 1). In that study it was suggested that the condensation of *N*-sulphonylated amino acids may involve formation of a mixture of products. The resulting oxazaborolidines[8] may form 1:1 adducts with either the *N*-sulphonylated amino acids, with aryl/alkyl boronic acids or with both of these. In addition, the loss of an aryl/alkyl group of the oxazaborolidine formed in the condensation reaction may take place in the presence of an *N*-sulphonylated amino acid.

Encouraged by the results obtained with *N*-tosyl-2-phenyl-1,3,2-oxazaborolidin-5-one **1b** we decided to subject a similar characterisation with **1a** (Scheme 1). Analogous intermediates and adducts may be involved in the formation of compound **1a**. The aim of this work was to detect anionic species involved in the formation of **1a** by ESIMS.

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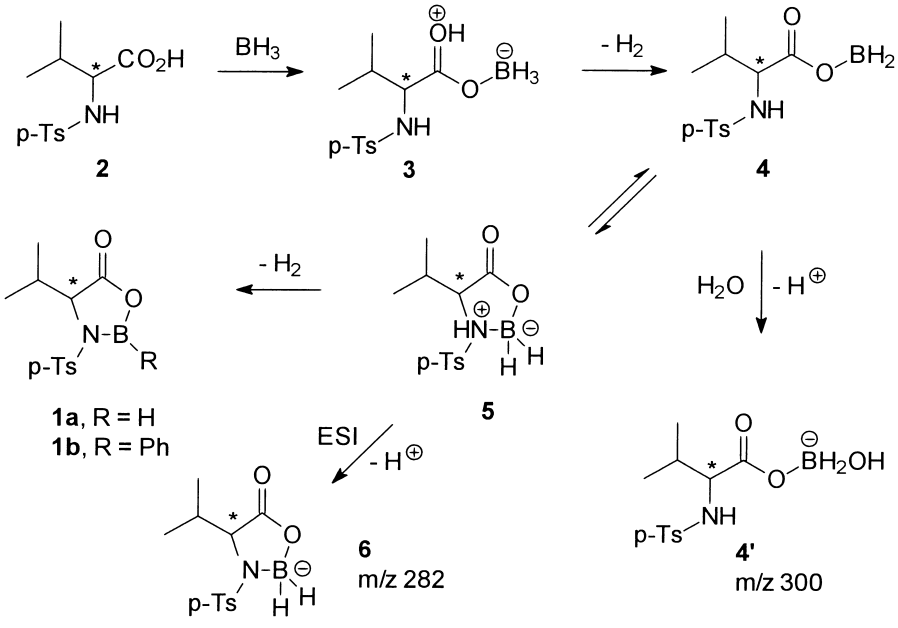
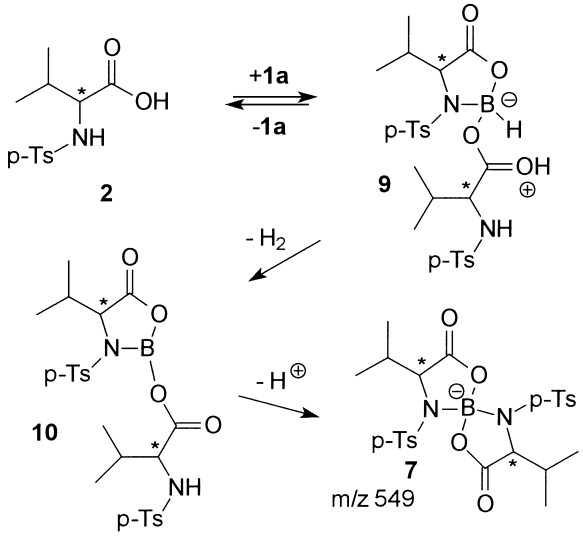


Scheme 1.

A crude product of **1a** was dissolved in acetonitrile and analysed with negative ion mode of ESIMS.[9] Indications of the formation of **1a** (intermediates **3**–**6**, Scheme 1) and a spiro adduct **7** (Scheme 2) were found.



Scheme 2.

2. Results and discussion

Anionic adducts **4′** (*m/z* 300, Scheme 1) and **6** (*m/z* 282) as well as the anion of acid **2** (*m/z* 270) were detected in the experiments.[10] Adducts of the anion of acid **2** with one or two molecules of **2** (anions *m/z* 541 and 812) were also observed, as it was the case in our earlier study.[8] The hydrogen

bonded adducts (anions *m/z* 541 and 812 in this study) are often formed at relatively high concentration during the process of electrospray ionisation at atmospheric pressure in the gas phase when the negatively charged droplets shrink and the charge density increases at the droplet surface. The suggested pathway (Scheme 1) starts with the reaction between Lewis acidic borane and the most Lewis basic site of the amino acid **2** to yield **3**. Hydrogen gas evolution from the intermediate **3** affords a boronate ester **4**. Anion **4′** (*m/z* 300) is probably formed when reactive boronate **4** reacts with residual amounts of water present in the solution. There was an apparent presence of water in the analysed solution, due to the acetonitrile used as a dilution solvent being only dried over molecular sieves. Intramolecular reaction on the boronate **4** generates a presumable intermediate **5** which was detected as its anion **6** (*m/z* 282) formed by charge separation within electrospray ionisation. Oxazaborolidinone **1a**, a supposed catalyst,[11] is produced when the intermediate **5** looses a hydrogen molecule. The route (Scheme 1) leading to **1a** is analogous to the condensation reaction between *N*-tosyl valine and phenyl boronic acid.[8] In contrast to the condensation reaction[8] involving proton rearrangements and losses of water molecules on the formation of **1b**, elimination of molecular hydrogen can be related to the generation of **1a** (Scheme 1).

The formation of spiro borate **7** (*m/z* 549, Scheme 2) involves an attack of amino acid **2** on the reactive oxazaborolidinone **1a** to generate adduct **9**. A loss of molecular hydrogen from the intermediate **9** affords boronate **10**. Deprotonation of **10** leads via an intramolecular reaction to a compound probably adopting the spiro structure **7**. We observed the same spiro borate **7** (via the loss of benzene instead of elimination of the hydrogen molecule, Scheme 2) in the crude product of **1b**.[8] It is interesting to note that Rose et al. also reported[12] intense signals of spiro borates with negative ESIMS, implying a relative stability of spiro borates at the low cone voltages used in ionisation.

3. Conclusion

The results presented herein indicate that ESIMS can be a convenient technique[9] for analysing labile compounds such as sensitive catalysts prepared in situ. As far as we know, this work together with the previous work[8] give the first published indications on the presence of oxazaborolidinones **1a** and **1b** which are assumed to serve as catalysts[11] in asymmetric Diels–Alder reactions. This work implies the formation of a mixture of products when *N*-sulphonylated amino acids react with borane. *N*-Tosyl-1,3,2-oxazaborolidin-5-one, as soon as it is produced, may form a 1:1 adduct with the starting amino acid.

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