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DIPLOMA THESIS

XANTHONE-BORONIC ACIDS: AN INSIGHT INTO THE SYNTHESIS OF BORYLATED XANTHONE DERIVATIVES

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Abstract – English

The development of Bortezomib **5** and discovery of its potential in the treatment of multiple myeloma has sparked hope, and a close attention is paid in medicinal chemistry to the synthesis of boronic acid derivatives as well as the evaluation of their anticancer, antimicrobial, and other activities. Parallelly, xanthones and xanthone derivatives are compounds thoroughly studied for their potential in the treatment of cancer, and their good antimicrobial, anti-inflammatory, antiviral and anticonvulsant activity. It is only natural that efforts are oriented towards the synthesis of xanthone boronic derivatives.

3,6-Dihydroxyxanthone **10** was chosen as a precursor for the development of a procedure to borylate xanthones, mainly due to its easy synthesis and availability. From **10**, 3,6-ditrifylxanthone **11** was easily prepared. The synthesis of 3,6-bis(pinacolatoboron)xanthone **8** from **11** was achieved using bis(pinacolatodiboron) B_2pin_2 as a borylation agent under $Pd(dppf)Cl_2$ catalysis with an addition of dppf complex in the presence of KOAc. A different procedure was explored by replacing B_2pin_2 with pinacolborane HBpin in the presence of Et_3N as base and higher yield was achieved. 3,6-Bis(pinacolatoboron)xanthone **8** was then deprotected into xanthone-3,6-diboronic acid (1**4**) by transformation of the pinacolboronate into a DEA-protected salt in the presence of diethanolamine, and byphasic (water/acetone) acidic hydrolysis of the obtained salt.

In an attempt to explore other borylation procedures, **10** was combined with NaH in the presence of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane in order to obtain 3,6-bis((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methoxy)-9H-xanthen-9-one **12** and consequently deprotect it into (((xanthone-3,6-diyl) bis(oxy))bis(methylene))diboronic acid **13**. However, the used conditions resulted in a partial reaction and 3-hydroxy-6-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methoxy)-9H-xanthen-9-one **12b** was obtained. Keeping in mind the extension of the borylation procedure to other xanthone derivatives, the synthesis of 2,7-dibromoxanthone **22** and 3,4-ditrifyl-1-methylxanthone **17** were attempted.