Drug Discovery Conference

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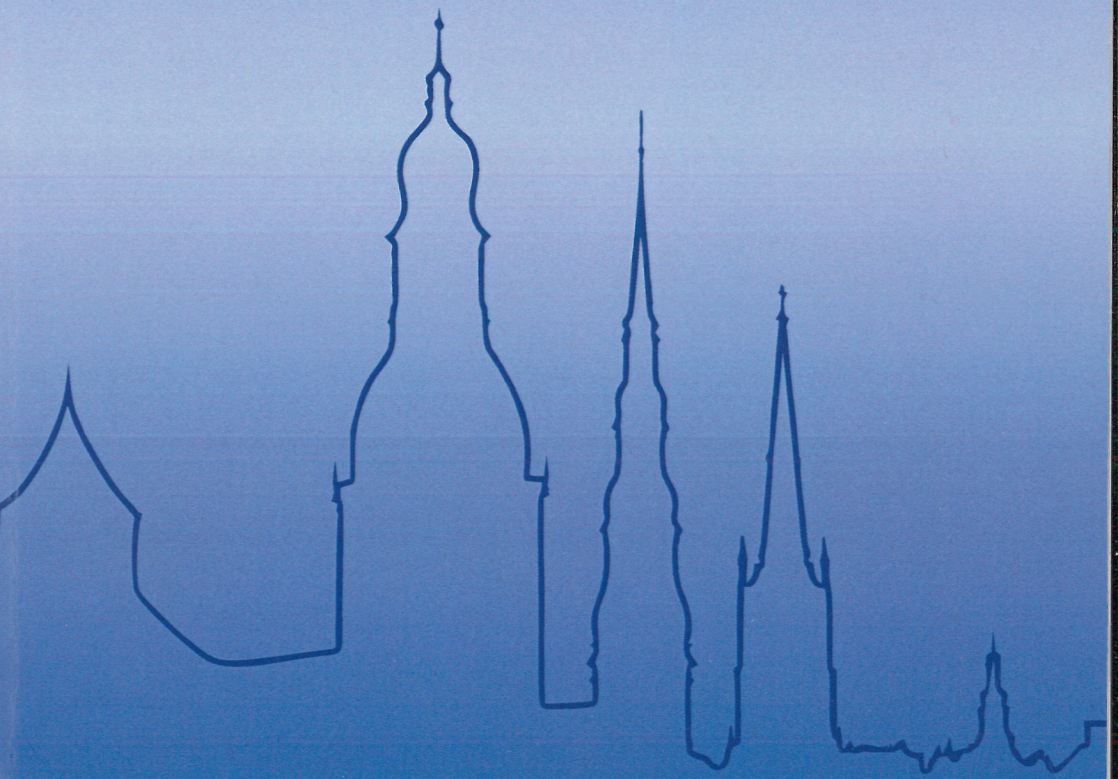

PP23. SACCHARIN DERIVATIVES AND SULFAMOYLBENZOIC ACIDS AS CARBONIC ANHYDRASE INHIBITORS

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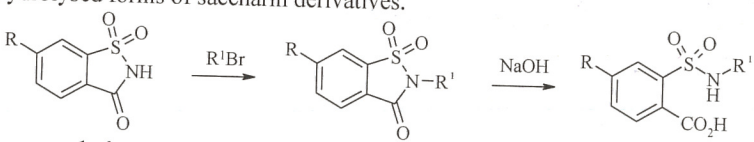
Carbonic anhydrases (CA) are zinc containing enzymes which catalyze CO_2 conversion to bicarbonate anion and control leading physiologic processes which are related to breathing and CO_2/bicarbonate transport between metabolising tissues and lungs, pH and CO_2 homeostasis, electrolyte secretion in tissues and organs, biosynthetic reactions.[1-2]

CAs are considered to be interesting targets for the design of pharmacological agents suitable for the treatment of various diseases.

The artificial sweetener saccharin (**1a**) and 6-sulfamoylsaccharin **1b** were reported as inhibitors of CA.[3-6]

The aim of this project was to synthesize a series of 2-alkylsaccharins **2a** and 2-alkyl-6-sulfamoylsaccharins **2b** and convert them to substituted mono- and disulfamoylbenzoic acid derivatives **3a** and **3b** via basic hydrolysis reaction. CA inhibitory activity was determined for both cyclic and hydrolysed forms of saccharin derivatives.



1a, b **2a, b** **3a, b**

a: R = H, **b**: R = SO_2NH_2
R^1 = Alkyl

The synthesis and CA screening results of substituted saccharins and sulfamoylbenzoic acids will be discussed.

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