

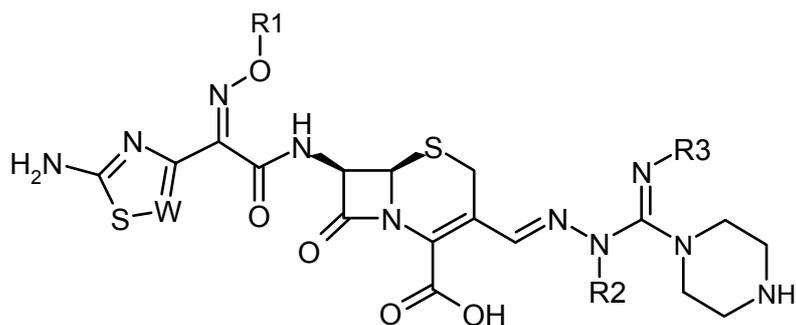
SYNTHESIS AND SAR (STRUCTURE ACTIVITY RELATIONSHIP) OF NOVEL BROAD SPECTRUM CEPHALOSPORINS INCLUDING MRSA-ACTIVITY

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We describe the synthesis and discuss the SAR of new parenteral cephalosporins (cephem-azomethines), which display highly improved activity against clinically relevant pathogens, i.e. MRSA (*methicillin resistant Staphylococcus aureus*), *Enterococcus faecalis* and *Enterobacter cloacae*. Until now, such activity was unknown for this class of compounds.

In general, the residue in position 7 was introduced by acylation of 7-amino-3-cephem-3-aldehyde with the heterocyclic acid chloride [1]. Condensation of the resulting hydroxylactone with aminoguanidines gives the desired cephalosporines. The most interesting compound found in this series, BC-1175 [2], was selected for further investigation.



BC-1175: W = N; R¹ = CH₂F; R² = Methyl; R³ = H

On a molecular basis, the corresponding IC₅₀-values obtained from measurements of the binding of these compounds to PBP2a (Penicillin Binding Protein 2a) will be given. A correlation to the *in vitro* MRSA activities is discussed.

[1] Gerd Ascher, Johannes Ludescher, Hubert Sturm, Josef Wieser; WO 9529182

[2] Gerd Ascher, Josef Wieser, Michael Schranz, Johannes Ludescher, Johannes Hildebrandt; WO 9843981