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论文

P-(3-酰氨基-4-取代苯基-2-吖丁啶酮基-1)-苯乙酸和P-(3-酰氨基-4-取代苯基-2-吖丁啶酮基-1)-苯乙酮的合成及抑制β-内酰胺酶作用

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摘要:

为研究吸电子基团远离环氮的单环β-内酰胺类化合物对β-内酰胺酶的抑制作用,设计与合成了21个新的p-(3-酰氨基-4-取代苯基-2-吖丁啶酮基-1)苯乙酸和p-(3-酰氨基-4-取代苯基-2-吖丁啶酮基-1)苯乙酮类化合物,经元素分析、红外光谱、核磁共振氢谱和质谱证实。生物活性测定表明,其中15个具有游离羧基的水溶性化合物对试验的腊样芽胞杆菌和绿脓杆菌产生的β-内酰胺酶有抑制作用。

关键词: 单环β-内酰胺 β-内酰胺酶抑制剂 p-(3-酰氨基-2-吖丁啶酮基-1)苯乙酸 p-(3-酰氨基-2-吖丁啶酮基-1)苯乙酮 2-吖丁啶酮

THE SYNTHESIS AND β-LACTAMASE INHIBITION ACTIVITY OF P-(3-AMIDO-4-SUBSTITUTED PHENYL-2-AZETI-DINONYL-1)-PHENYLACETIC ACIDS AND P-(3-AMIDO-4-SUBSTITUTED PHENYL-2-AZETIDINONYL-1)-ACETOPHE-NONES

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Abstract:

In order to investigate the effects of the N-substituents which the electron-withdrawing groups are far-away from the nitrogen atom of the β-lactam ring on the β-lactamases inhibition activities, twenty one title compounds have been synthesized from methyl p-amino-phenylacetate and p-amino-acetophenone. Condensation between "Dane Salt" and azomethines carrying an ester function or an acetyl group in the presence of ethyl chloroformate and triethylamine leads to stereo-specific synthesis of cis-3-enamino -2-azetidinones in about 10-50% yield. The 3-amino protective group can be easily removed with hydrochloric acid in 80～90% yield. The 3-amide-β-lactam-esters on treatment with 0.1N NaOH in acetone give a free carboxyl group in 50-70% yield without affecting the β-lactam ring or the amido side chain. The structure of these β-lactams were confirmed through their elemental analysis, IR, ^{1}HNMR and MS spectra. The β-lactamase inhibition activity test in vitro showed that fifteen title compounds carrying a free carboxyl function far-away from the ring nitrogen atom have inhibitory activity against two β-lactamases produced by P. aeruginosa, and Acetobacter respectively.

Keywords: β-Lactamase inhibitor p-(3-Amido-2-azeti-dinoyl-1)-phenylacetic acid p-(3-Amido-2-azetidingnyl-1)-acetophenone 2-Azetidinone Monocyclic β-Lactam

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