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石杉碱甲-AChE复合物中石杉碱甲的结构特征: 量子化学研究

朱维良,蒋华良,陈建忠,顾健德,刘东祥,林茂伟,陈凯先,嵇汝运,曹阳

中国科学院上海药物研究所;中国科学院新药研究国家重点实验室;苏州大学化学化工学院

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摘要 在运用量子化学从头计算方法(HF/4-31G)结合点电荷模型方法对AChE-HupA复合物活性位点的410个原子和1929个点电荷进行理论计算的基础上,
比较了石杉碱甲分子在形成复合物前后的结构变化特征。发现复合物中石杉碱甲分子构象并非能量最低构象,它的能量比HF/4-31G全优化得到的构象的能量高91.8kj/mol。和单分子状态相比,
形成复合物后季铵基和内酰胺基的N-H, C=O键的键长变长、键强减弱,
其总原子净电荷也发生了明显的变化。且这些基团的空间取向都有不同程度的改变, C(8)-N(21)键的旋转达20 iii。这些信息将有益于设计新的AChE抑制剂。

关键词 生物碱 从头计算法 石杉碱甲

分类号 0641

Characteristics of huperzine a structure in huperzine a-acetylcholinesterase complex : A quantum chemistry study

ZHU WEILIANG,JIANG HUALIANG,CHEN JIANZHONG,GU JIANDE,LIU DONGXIANG,LIN MAOWEI,CHEN KAIXIAN,JI RUYUN,CAO YANG

Abstract The difference between Huperzine A (HupA) structure in Acetylcholinesterase (AChE)-HupA complex and the structure in gase phase has been studied by using ab initio method of quantum chemistry. The model system composed of 410 atoms abstracted from the active site of HupA-AChE complex and of the 1929 point charges around the 410 atoms was calculated employing HF/4-31G method. The HupA itself in gase phase state was optimized with HF/4-31G. The calculation result indicated that the binding conformer and the global minimal energy conformer of HupA is 91.8kJ/mol. The changes of LUMO and HOMO energies indicate that the electrons were transferred between AChE and HupA. Great changes have been taken palce for the total atomic charge, bond lengthes and orientations of some of the atoms and bonds in HupA when it binds to the AChE: the C=O and N-H bond of amide group and the N-H bond of the amino group of HupA have been elongated and weakened in HupA-AChE complex, the torsion angle of bond C(3)-C(8)-N(21)-H(35) alters even about 20iii. These changes are caused by the hydrogen bonds formation between HupA and AChE. All of these are useful clues for designing novel huperzine A analogs to inhibite the activity of acetylcholinesterase.

Key words ALKALOID AB INITIO CALCULATION

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通讯作者