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含氟农药的比较分子场分析研究

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摘要 用比较分子场分析(CoMFA)方法对112种含氟农药分子的生物活性及毒性同时进行了定量构效关系研究。用78个化合物作为训练集，以距离比较方法(DISCO)确认的药效团为叠合规则构建CoMFA模型，发现影响活性的立体场与静电场的贡献分别为60.4%和39.6%，影响毒性的立体场与静电场的贡献分别为59.2%和40.8%。药效模型与毒效模型在交叉验证时的相关系数平方(R^2)分别为0.652和0.611，非交叉验证的R^2分别为0.982和0.977，方差比F(8,69)值分别为463.6及362.9，活性和毒性的标准偏差-极差比s/△ɣ值分别为3.6%和2.9%，表明模型具有较好的自预测能力。对测试组34个化合物进行了活性和毒性的预测，活性与毒性预测的标准偏差-极差比s/△ɣ值分别为10.4%和6.4%。最后，还建立了一个由97个化合物构建的扩大的模型，各种统计量得到了进一步提高。并预计了一个活性较高且毒性很低的新化合物。

关键词 农药 氟化合物 定量构效关系 三维结构

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3D-QSAR study of flurine-containing pesticides

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Abstract The quantitative structure-activity/toxicity relationships (QSAR/QSTR) of 112 fluorine-containing pesticides were studied by means of the DISCO and CoMFA method. Using the 78 compounds among them chosen randomly as a training set to build up the QSAR/QSTR model, it is found that the contribution to activity from steric effect is 60.4%, and that from electrostatic effect is 39.6%. As to the QSTR model, the contribution from steric effect is 59.2%, and that from electrostatic effect is 40.8%. The crossvalidated R^2 are 0.652 and 0.611, and the non-crossvalidated R^2 are 0.982 and 0.977, and the values of variance ratio F ar 463.6 and 362.9 for the activity and the toxicity respectively. It was proved that the two models make good prediction for activity and toxicity. These models are also used to predict the activities and toxicities of other 34 compounds in the test set. The values of ratio of standard error and extremal length obtained, s/△ɣ, are 10.4% and 6.4% for activity and toxicity respectively. Finally these models are improved by adding more compounds into the training set. A new molecule with higher activity and lower toxicity is designed using the last model.

Key words PESTICIDES FLUORINE COMPOUNDS QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP THREE DIMENSIONAL STRUCTURE

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