Influence of the p-substituent for the Diastereomeric Resolution of Carboxylic Acids

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The salts of (S)- and (R)-1,4-benzodioxane-2-carboxylic acid with three (S)-1-arylethylamines have been investigated [1]. Their melting points and their solubilities in alcoholic solvents revealed large differences between the benzodioxanecarboxylates of (S)-1-(p-nitrophenyl)ethylamine and (S)-1-(p-methylphenyl)ethylamine. Therefore this latter amines were selected to resolve (±)-1,4-benzodioxane-2-carboxylic acid by diastereoselective crystallisation finding that both of them display a high resolution ability for such substrate, which contrasts with the null efficiency of unsubstituited 1-phenylethylamine. The crystal structures of the salts showed that there is correlation between the efficiencies of the optical resolutions of the amines with the resolving reagents and the crystal structures of the salts. A hydrogen bond layer was found to be common to the less soluble salt crystals, consisting of stable columnar structures with planar boundary surface [2]. In contrast, in the corresponding more soluble salts no particularly stabilized crystal structure is formed, only columnar structures are present. There results strongly suggest, that for successful resolution it is necessary realize hydrogen bond layers, consisting of stable columns with planar boundary surfaces, in the crystal of one of the pairs of diastereomeric salts

[1] Bolchi C., Pallavicini M., Fumagalli L., Marchini N., Moroni B., Rusconi C., Valoti E., *Tetrahedron Asymmetry,* 2005, *in press.* [2] Kinbara K., Sakai K., Hashimoto Y., Nohira H., Saigo K., *J. Chem. Soc. Perkin Trans*, 1996, **2**, 2615.

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