

Abstract

SYNTHETIC STUDIES CONNECTED WITH THE PREPARATION OF *N*-[3-(3-CYANOPYRAZOLO[1,5-*a*]PYRIMIDIN-5-YL)PHENYL]- *N*-ETHYLACETAMIDE, A ZALEPLON REGIOISOMER

Rigorous Thesis

Mgr. Michaela Blahovcová

Charles University in Prague, Faculty of Pharmacy in Hradec Králové,
Department of Pharmaceutical Chemistry and Drug Control,
Heyrovského 1203, Hradec Králové

This thesis is a continuation of my master thesis and further develops the subject of zaleplon impurities. The main subject of the work is the zaleplon regioisomer, *N*-[3-(3-cyanopyrazolo[1,5-*a*]pyrimidin-5-yl)phenyl]-*N*-ethylacetamide called isozaleplon, which is the most problematic impurity of zaleplon.

The purpose of this thesis was to propose a synthetic way leading to isozaleplon based on the available literature. Then this substance was intended to be used as a standard for determination of this impurity in preparation of zaleplon by various methods.

The studied approaches to the isozaleplon synthesis were based on Suzuki-Miyaura cross-coupling reaction of the corresponding boronic acids and/or boronates, mainly with 5-chloropyrazolo[1,5-*a*]pyrimidin-3-carbonitrile. Various methods of preparation of both components are described, as well as approaches based on the final modification of the 5-(3-aminophenyl)-pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile moiety prepared by Suzuki-Miyaura cross-coupling. All the prepared compounds were identified by NMR techniques. Spectral characteristics (IR, UV, MS) of these compounds are also given.

At the end of this thesis, a study of different modifications of zaleplon synthesis and comparison of the HPLC impurity profiles of the corresponding products is given.