ABSTRACT

Syntheses of angiotensin convertases TCV-116, which are used for treatment of hypertension and other related cardiovascular diseases, mostly differ in reaction sequence. In general, there is benzimidazole part, biphenyltetrazole ring, and ester side chain. This research includes two different ways to prepare one of the main precursors for the synthesis of TCV-116. High resolution mass spectrometry hyphenated to high performance liquid chromatography was used to detect all present organic impurities in samples, prepared *via* two different synthetic strategies. Based on mass spectra and fragmentation patterns I have proposed chemical structures (structure) to each impurity detected and regarding target mass search in previous steps of synthesis I have determined its origin. Special attention to process-related organic impurities was given since degradation impurities are more or less known. Based on Further, I have proposed mechanism of occurrence for each impurity and confirmed its structure via target synthesis and isolation or by simple stress tests. I have found that majority of impurities develop during last or penultimate step of process in both cases. In first scenario, the last synthetic step is esterification, where 1-chloroethylcyclohexyl carbonate is added to generate key precursor. I have determined most impurities form out of impurities, present in reagent 1-chloroethyl cyclohexyl carbonate. By GC-MS screening, related substances were identified in this reagent. Because of structure analogy to key intermediate, impurities are difficult to remove. In the second synthesis, the largest number of impurities generates during Suzuki coupling reaction. Apparently, tetrazole synthesis and trityl protection formation do not remove the rest of impurities. I have shown that with high resolution mass spectrometer impurity traces can be identified and that target mass search can help discover cause or source for its creation. I have also shown structure confirmation can be done by simple stress tests. These results may have some potential applications in structural analysis of common compounds by mass spectrometry and could introduce some tips for synthesis of key precursor for angiotensin convertases inhibitor. Some identified impurities presence in key precursor can represent potential risk for users health, because are hazardous and can cause DNA damage due its reactivity.

Keywords: High resolution mass spectrometry, angiotensin convertases inhibitor, key precursor, organic impurities.