Abstract: For the first time, quantitative LC-MS/MS profiling of 56 hop-derived sensometabolites contributing to the bitter taste of beer revealed a comprehensive insight into the transformation of individual bitter compounds during storage of beer. The proton-catalyzed cyclization of trans-iso-alpha-acids was identified to be the quantitatively predominant reaction leading to lingering, harsh bitter tasting tri- and tetracyclic compounds such as, e.g. the cocongeners tricyclocohumol, tricyclocohumene, isotricyclocohumene, tetracyclocohumol, and epitetracyclocohumol, accumulating in beer during storage with increasing time and temperature. The key role of these transformation products in storage-induced trans-iso-alpha-acid degradation was verified for the first time by multivariate statistics and hierarchical cluster analysis of the sensomics data obtained for a series of commercial beer samples stored under controlled conditions. The present study offers the scientific basis for a knowledge-based extension of the shelf life of the desirable beer's bitter taste and the delay of the onset of the less preferred harsh bitter aftertaste by controlling the initial pH value of the beer and by keeping the temperature as low as possible during storage of the final beverage.