

ROTATIONAL SPECTRUM AND CARBON ATOM STRUCTURE OF DIHYDROARTEMISINIC ACID

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Dihydroartemisinin acid (DHAA, C₁₅H₂₄O₂, five chiral centers) is a precursor in proposed low-cost synthetic routes to the antimalarial drug artemisinin. In one reaction process being considered in pharmaceutical production, DHAA is formed from an enantiopure sample of artemisinin acid through hydrogenation of the alkene. This reaction needs to properly set the stereochemistry of the asymmetric carbon for the synthesis to produce artemisinin. A recrystallization process can purify the diastereomer mixture of the hydrogenation reaction if the unwanted epimer is produced in less than 10% abundance. There is a need in the process analytical chemistry to rapidly (less than 1 min) measure the diastereomer excess and current solutions, such as HPLC, lack the needed measurement speed. The rotational spectrum of DHAA has been measured at 300:1 signal-to-noise ratio in a chirped-pulsed Fourier transform microwave spectrometer operating from 2-8 GHz using simple heating of the compound. The ¹³C isotope analysis provides a carbon atom structure that confirms the diastereomer. This structure is in excellent agreement with quantum chemistry calculations at the B2PLYPD3/6-311++G** level of theory. The DHAA spectrum is expected to be fully resolved from the unwanted diastereomer raising the potential for fast diastereomer excess measurement by rotational spectroscopy in the pharmaceutical production process.