DIKETO-KETOENOL TAUTOMERS IN CURCUMINOIDS

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Curcumin represents a class of natural drugs possessing wide range of pharmacological properties including anti-inflammatory and anti-oxidant activities.[1,2] Curcumin and its derivatives exist in an equilibrium between diketo and ketoenol tautomers. Each of the tautomeric states exhibits dissimilar potency to bind biomacromolecules which affects their pharmacological activities.[3]

In this work, we present comprehensive NMR studies of curcumin analogues in different solvents. We described equilibrium properties of curcumin and its 12 derivatives including pharmaceutical ingredient ASC-JM17 (**1**, Figure 1) in different solvents. Moreover, we separated two tautomers of ASC-JM17 on column chromatography and studied their equilibration in solution. Solid-state NMR and X-ray diffraction studies revealed two new polymorphs of ketoenol tautomer of ASC-JM17 (**1KE**, Figure 1).

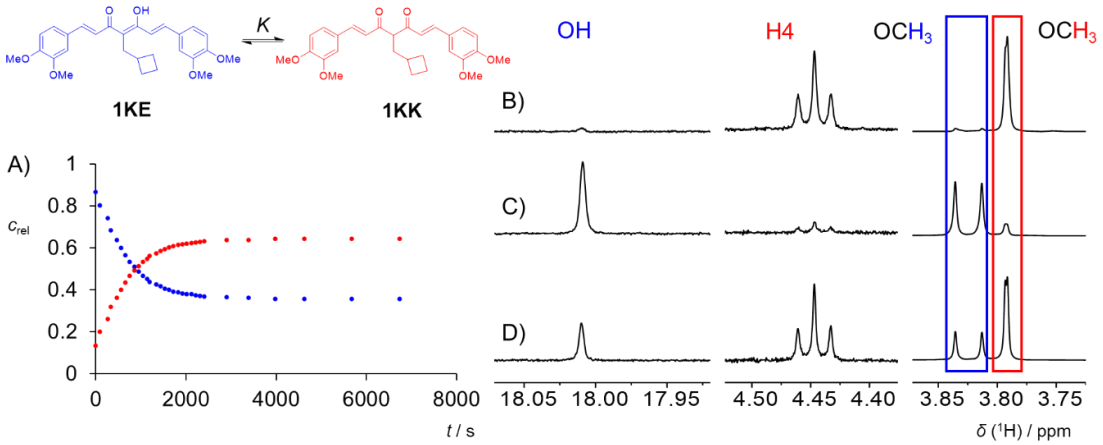

Figure 1. A) The keto-enol equilibrium of compound **1** and the time-dependence of relative concentration, c_{rel}, of **1KK** and **1KE** obtained from ^{1}H NMR spectra after dissolution of the pure **KE** form. The OH, H4 and methoxy-group region of ^{1}H NMR spectra of B) lyophilizate containing over 95 % of the **KK**, C) the crystalline **1KE** and D) the equilibrium mixture in d_6-DMSO at room temperature. Note that the first NMR experiment, t = 0, was recorded about 3 minutes after dissolution of the compounds.

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