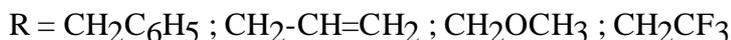
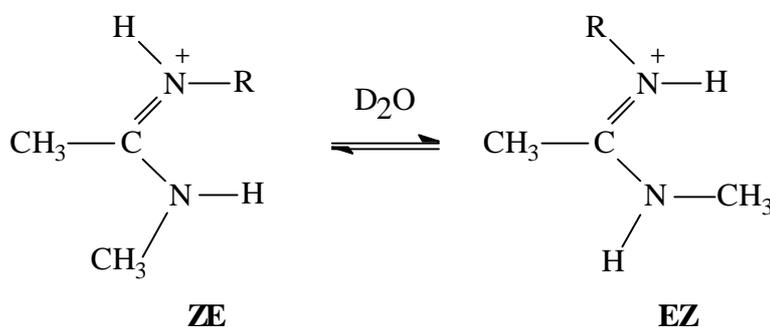


## N-Alkyl-N-methylacetamidinium Ions. Isomerization and Water Catalyzed Exchange Rates in D<sub>2</sub>O

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Previously we had reported results on the rate of stereoisomerization (see figure) in D<sub>2</sub>O of N-benzyl-N'-methylacetamidinium ion in an ample pD range (D<sub>2</sub>O is used as a solvent).



We found that the sigmoided-type profile of  $k_{\text{obs}}$  vs. pD plot, fits the rate expression :  $k_{\text{obs}} = (k_1[\text{D}^+] + k_2K_a) / (K_a + [\text{D}^+])$ , where  $k_1$  and  $k_2$  are the rates of isomerization of the acetamidinium ion and the acetamide respectively and  $K_a$  is the acidity equilibrium constant of the acetamidinium ion. These constants were evaluated by measuring the rates at each pD using dynamic NMR(H) (line shape analysis and saturation transfer). Based on the low barrier of 19.7 Kcal/mol at 25°C ( $k_1 = 0.02 \text{ s}^{-1}$ ) it was suggested that the isomerization (EZ-ZE) of the acetamidinium form proceeds through rotation of the C-N partial double bond. We argued that this relatively low barrier is due to the steric repulsion of the N-benzyl group that destabilizes the ground state (planar amidinium) relative to its twisted transition state. On the other hand, our result supports that the E-syn-Z-anti isomerization of the acetamide form proceeds via rotation about a C-N single bond as it had been proposed previously. We stated that the proposed mechanism was in agreement with the measured low barrier of 14.7 Kcal/mol at 25°C ( $k_1 = 126 \text{ s}^{-1}$ ). In order to test the proposed mechanisms and in view of the biological importance of the acetamides we have undertaken a systematic study on the isomerization of N'-alkyl-N-methylacetamides as a complementary support to our previous results on the N-benzyl-N'-methylacetamide. Therefore we have prepared the following acetamides: N-allyl-N'-

methylacetamide ( $R=CH_2-CH=CH_2$ ), N-trifluoroethyl-N'-methylacetamide ( $R=CH_2CF_3$ ) and N-methoxyethyl-N'-methylacetamide ( $R=CH_2OCH_3$ ). The purpose of this study is to measure the isomerization rates under pD conditions in which both forms, acetamidinium ion and acetamide, participate. Therefore, the rates  $k_1$  and  $k_2$  and the equilibrium,  $K_a$  of each of these compounds was determined. We then explore the existence of a structure-reactivity relationship for each parameter. Finally we search on the rate of proton exchange, at low pD, where  $D_2O$  acts as a base and we found the relative acidity between the  $-NH$  sites at the acetamidinium ions.