A STUDY OF OMEPRAZOLE BEHAVIOR

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Omeprazole is a substituted benzimidazole which suppress de acid-gastric secretion by H+, K+-ATPase enzyme inhibition. It presents an optically active center located on the sulfur atom from the sulfoxide group. Omeprazole is a pro-drug and thus it is not exactly the active inhibitor of the enzyme, which produces the acid-gastric secretion. It is easily converted in its respective sulfenamide, which has not optical activity, at low pH. [1] Figure 1 shows the decomposition reaction from omeprazole (**1**) to sulfenamide (**4**). Besides, omeprazole has some rotational freedom.

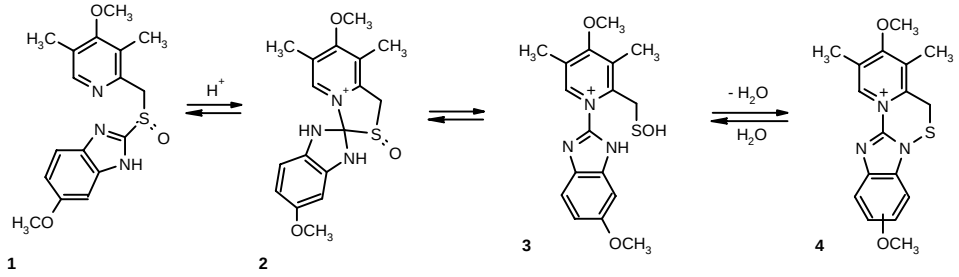

Figure 1. Omeprazole decomposition reaction in acid medium.

The main goal of this work is to study the behavior of omeprazole based on its characteristics discussed above. By observing the molecule flexibility, a conformational analysis was performed to find the minimum energy structures. Quantum chemistry coupled to chemometric methods were used.[2] The racemization barrier for every minimum energy structures was determined using the semi-empirical PM3 method. The total energy involved in the decomposition reaction was also calculated by ab-initio method at Hartree-Fock level using a 6-31G** basis set. From the conformational study, three minimum energy structures were found with energy around -35 kcal mol^{-1}. For racemizations barriers, the value found was around 43 kcal mol^{-1} whereas for the decomposition reaction the total energy found was -266. 78 kcal mol^{-1}.

1. A) M. Tanaka, H. Yamazaki, H. Hakusui, N. Nakamichi, H. Sekino, *Chirality*, **9**,17 (1997). B) B. D. Landes, J. D. Petite, B. Flouvat, *Clin. Pharmacokinet*, **28**,1158 (1995). C) P. Lindberg, P. Nordberg, T. Alminger, A. Brändström, B. Wallmark, *J. Med. Chem.*, **29**,1329 (1986).
2. A. T. Bruni, V.B.P. Leite, M.M.C. Ferreira, *J. Comp. Chem.*, accepted.

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