Cover Profile
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Rotation-Inversion Isomerization of Tertiary Carbamates: Potential Energy Surface Analysis of Multi-Paths Isomerization Using Boltzmann Statistics

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The front cover artwork is provided by Prof. Rainer Glaser's group at the Missouri University of Science and Technology. The image shows one of four potential energy surfaces generated from our rotation-inversion study of tertiary carbamates and highlights two of the eight possible transition state pathways between two ensembles of *E*- and *Z*-minima. In the context of synthetic studies of fluorinated carbamates $R_1O-CO-N(R_2)CH_2CF_3$, we unexpectedly observed two sets of ^{13}C NMR quartets for the CF_3 group and we needed to understand their origin. Read the full text of the Research Article at 10.1002/cphc.2022005442.

What is the most significant result of this study?

We were able to show that the two sets of CF3 NMR quartets are due to the presence of ensembles of E- and Z-rotamers. A fully consistent interpretation is proposed and supported by the results of a complete stereochemical analysis, the exploration of all isomerizations with focus on the rotation-inversion, and the computation of chemical shifts $\delta(^{13}C)$ and $^1J(^{13}C,^{19}F)$ coupling constants. More generally, the approaches described in our study will facilitate similar studies of rotation-inversion dynamics in carbamates $R_1R_2N-CO-OR_3$ and ureas $R_1R_2N-CO-NR_3R_4$.

What was the inspiration for this cover design?

The rotation-inversion pathways of carbamates inherently present a two-dimensional problem and deep understanding requires plots of the rotation-inversion surfaces as a function of parameters describing CN rotation and *N*-inversion. Four such surfaces were determined, and we chose to highlight the surface that features the most stable minima and most traversed TS structure. Negative hyperconjugation is key to understanding the electronic structure of the TS structures.

What was the biggest challenge on the way to the results presented in this paper?

The analysis of our computational model showed **eight** TS structures connecting **four** *E*- and *Z*-minima. This scenario required a clear conceptual approach to predict the barrier that would be experimentally measured. The Boltzmann analysis shows that all eight isomerization paths are travelled, and the application of proper statistics resulted in a computed barrier which was in complete agreement with the experimentally determined barrier of a very similar fluorinated carbamate, *N*-Boc-*N*-(2,2,2-trifluoroethyl)-4-aminobutan-1-ol **II** (within 1%).

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