

 CLUSTER SPECTROSCOPY

Fluorine gets friendly

Solvents are an indispensable part of the chemist's toolbox, providing the medium for almost all of organic chemistry to take place. Trifluoroethanol (TFE) is commonly used as a co-solvent with water for protein folding studies. However, when mixed with water, TFE displays some unusual behaviour, such as the formation of small self-aggregates, leading to incomplete mixing of the two solvents at the microscopic scale. We do not yet know the precise structure of these aggregates, but they are expected to strongly influence the behaviour of these co-solvents and their solutes. Now, writing in *Angewandte Chemie International Edition*, Yunjie Xu and co-workers have used rotational spectroscopy, coupled with first-principles calculations, to shed light on the intermolecular interactions governing the behaviour of TFE on its first steps towards aggregation in the condensed phase.

The TFE molecule can exist in three conformations: *gauche*(+), *gauche*(−) and *trans*. “One particular phenomenon that drew our attention is that the *trans* configuration of TFE appears to be unstable when isolated in the gas phase,” explains Xu, “whereas the *trans:gauche* ratio increases to 40:60 in the liquid state.” In order to understand this change, the researchers posed a simple question: what is the minimum cluster size in which the *trans* conformation of TFE emerges? Addressing the problem directly, Xu and her team produced different-sized TFE clusters in a pulsed molecular expansion and analysed them using chirped pulse microwave spectroscopy, a highly sensitive technique that allowed them to probe the individual

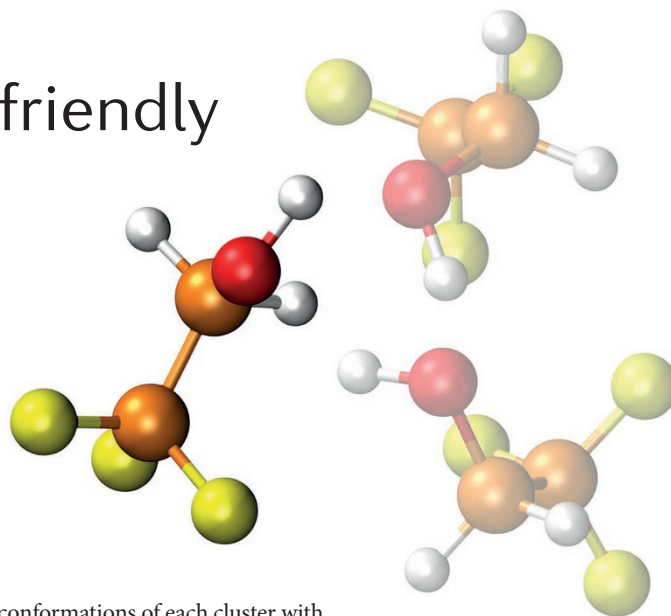


Image courtesy of Y. Xu, University of Alberta, Canada.

conformations of each cluster with unprecedented precision.

Surprisingly, in clusters of only three molecules (trimers), they found that the dominant intermolecular configuration already contained one *trans*-TFE subunit. This is in contrast to earlier work on 2-fluoroethanol (FE): although FE can display similar hydrogen bonding interactions to TFE, each FE molecule within a trimer preferentially adopts a *gauche* conformation.

In order to disentangle the intermolecular contributions that stabilize the TFE clusters, Xu and her team carried out quantum mechanical calculations and an electron density analysis of the non-covalent interactions. They found that the all-*gauche* configuration, as in FE, would be the most stable in the TFE trimer if hydrogen bonding were the only intermolecular interaction involved. Instead, they discovered that additional attractive weak F...F halogen bonds were decisive in preferentially stabilizing the *trans* conformation of a TFE subunit in the trimer.

“This finding is somewhat counterintuitive as chemists often emphasize the repulsive nature of the F...F interaction,” notes Xu. In addition to these simple pairwise

interactions, they discovered a previously unobserved three-body F...F...F stabilizing interaction in the trimer. However, despite finding that halogen bonding is the crucial factor that stabilizes the *trans* conformation of TFE in the trimer, Xu's team still have not been able to reproduce the *trans:gauche* ratio of 40:60 observed in the liquid phase.

“To reach the *trans:gauche* ratio of 40:60 in the liquid phase, one needs to go beyond the ternary TFE clusters,” concludes Xu. With that in mind, Xu and her team now intend to investigate larger TFE clusters, as well as mixed TFE–water systems. Are such exotic halogen bonding interactions of equal importance here?

Adam West, Associate Editor,
Nature Communications

ORIGINAL ARTICLE Thomas, J. et al. A direct link from the gas to the condensed phase: a rotational spectroscopic study of 2,2,2-trifluoroethanol trimers. *Angew. Chem. Int. Ed.* <http://dx.doi.org/10.1002/anie.201612161> (2017)

FURTHER READING Thomas, J. et al. Unusual H-bond topology and bifurcated H-bonds in the 2-fluoroethanol trimer. *Angew. Chem. Int. Ed.* **54**, 11711–11715 (2015)