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COMMENT

Comment on “Theoretical investigations into the enantiomeric and racemic forms of α -(trifluoromethyl)lactic acid” by R. Tonner, V. A. Soloshonok and P. Schwerdtfeger, *Phys. Chem. Chem. Phys.*, 2011, **13**, 811-817

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It is argued that differences between homo- and heterochiral dimers of the title compound in the gas phase cannot be responsible for the different sublimation behaviour of racemic and enantiomerically pure crystals near room temperature.

In a recent publication in this journal,¹ a detailed quantum-chemical study of α -(trifluoromethyl)lactic acid (TFMLA) aggregates is presented. It extends well beyond an earlier study used to support infrared spectra of TFMLA and its dimers in supersonic jets² (ref. 80 in ref. 1). The quantum chemical results indicate a slight preference for the most stable heterochiral dimer structure in the gas phase compared to the most stable homochiral dimer, thus confirming the lower level result obtained before.²

In contrast to the authors of ref. 1, we would argue that this slight preference is irrelevant for the observed preferential sublimation of racemic TFMLA near room temperature, because dimers are not present in significant amounts in the gas phase under such conditions. Rather, the sublimation preference must be rooted in the properties of the solid state alone,^{2,3} as in related cases.^{4–6}

First of all, it was shown experimentally² that most of the sublimation selectivity of TFMLA is of thermodynamic origin,⁷ rather than kinetically controlled. Therefore, only the equilibrium vapor and solid phases have to be analyzed. For the dimerization equilibrium $2M \rightleftharpoons D$, the dimensionless equilibrium constant K_p can be written as $K_p = p_D p^\circ / p_M^2$ with the standard pressure $p^\circ = 1$ bar and the partial pressures p_M and p_D of the monomer M and the dimer D.

In terms of the dimer/monomer ratio p_D/p_M , this means $p_D/p_M = K_p p_M / p^\circ$. By analogy to the slightly less volatile benzoic acid case, where the vapor pressure reaches 10^{-3} bar only around 370 K,⁸ one can safely exclude a vapor pressure of TFMLA at 300 K in excess of 10^{-4} bar. Actually, we estimate the room temperature vapor pressure $p_M \approx 5 \times 10^{-5}$ bar from a gas phase cell measurement² and comparison to the calculated IR band strength. Therefore, the dimerization

constant K_p would have to exceed 10^3 in order to lead to a significant ($>10\%$) dimer fraction near room temperature. This is clearly not the case, as shown by a comparison to other carboxylic acids, for which it has been determined accurately.^{9,10} The change of $K_p(300\text{ K})$ with chemical substitution is modest, because the standard Gibbs energy is determined by the rather uniform standard enthalpy of dimerization of carboxylic acids¹¹ and the similarly uniform standard entropy of dimerization.¹² At higher temperatures, the vapor pressure increases, although this increase and therefore the growing importance of dimers is somewhat attenuated by a decrease in the dimerization constant. However, it was experimentally established that the vapor pressure difference between enantiomerically pure and racemic TFMLA is already large at room temperature.² All this rules out a significant role of dimers in the vapor pressure difference of TFMLA samples of different enantiomeric purity.

The authors in ref. 1 could actually use their high quality computed free enthalpies for the dimers and monomers to estimate the gas phase equilibrium constant in the rigid rotor and harmonic oscillator approximation.¹³ One can be confident that their data will predict an equilibrium constant on the order of 10^2 , well below that needed to form substantial amounts of dimers at the equilibrium vapor pressure near room temperature.

There is also independent experimental support from room temperature gas phase spectra that p_D/p_M is less than 0.1,² because otherwise there would be spectroscopic evidence for the dimer vibrations at room temperature (see Fig. 3 and 5 in ref. 2). We wish to point out that these dimers do exist and can be prepared in supersonic jets.² They are simply not favored under conditions of room temperature thermodynamic equilibrium with the solid. In this context, it should be emphasized that dimers connected by the α -hydroxy group (dimer B in ref. 1) are not relevant in the gas phase because of their high energy¹ and they are consequently not observed.²

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Finally, one could argue with Occam's razor. While racemic crystals of TFMLA still have a narrow stability range, such racemic compounds are not stable at all in the so-called conglomerate formers.¹⁴ As a consequence, volatile conglomerate formers show thermodynamically controlled enantio-enrichment from the very first excess molecules in the solid,² because S- and R-configured molecules evaporate independently with the same likelihood, thus leaving any initial enantiomeric excess behind, if the size of the vapor phase is chosen appropriately. When going through a list of these conglomerate formers,⁵ even focussing on the most volatile ones, one does not notice a propensity for typical gas phase dimer formers such as monocarboxylic acids. Quite in contrast, one finds many multifunctional molecules in the list which tend to form intermolecular networks and will definitely not evaporate as dimers. Therefore, conglomerate formation as an extreme disposition for self-disproportionation does not correlate with gas phase dimerization. On the other hand, there are definitely gas phase dimers with much more pronounced chirodiastaltic effects than TFMLA,¹⁵ but with less pronounced crystal vapor pressure differences, such as methyl mandelate.¹⁶ This empirical lack of correlation suggests that gas phase dimers are unlikely to play a systematic role in explaining vapor pressure differences between enantiomerically pure and racemic solids.

The combination of weak chirality recognition¹⁵ in carboxylic acid dimers (an energy argument) and weak dimerization propensity in all but the most volatile carboxylic acids¹¹ (an entropy argument) rules out a significant vapor phase influence on the sublimation behaviour of TFMLA at environmental temperatures. In contrast to the conclusion drawn in ref. 17 and rather unspectacularly, the thermodynamic stability of the crystal must be decisive. This allows to focus the theoretical treatment on this challenging task.¹ It is

exciting to see the progress which theoretical chemistry is making towards the accurate *ab initio* prediction of such subtle crystal forces.¹⁸

References

- 1 R. Tonner, V. A. Soloshonok and P. Schwerdtfeger, *Phys. Chem. Chem. Phys.*, 2011, **13**, 811–817.
- 2 M. Albrecht, V. A. Soloshonok, L. Schrader, M. Yasumoto and M. A. Suhm, *J. Fluorine Chem.*, 2010, **131**, 495–504.
- 3 D. G. Blackmond and M. Klussmann, *Chem. Commun.*, 2007, 3990–3996.
- 4 J. S. Chickos, D. L. Garin, M. Hitt and G. Schilling, *Tetrahedron*, 1981, **37**, 2255–2259.
- 5 J. Jacques, A. Collet and S. H. Wilen, *Enantiomers, Racemates, and Resolutions*, John Wiley and Sons, 1981.
- 6 M. Albrecht, J. Will and M. A. Suhm, *Angew. Chem., Int. Ed.*, 2010, **49**, 6203–6206.
- 7 P. Cintas, *Angew. Chem., Int. Ed.*, 2008, **47**, 2918–2920.
- 8 D. R. Stull, *Ind. Eng. Chem.*, 1947, **39**, 517–540.
- 9 J. V. Auwera, K. Didriche, A. Perrin and F. Keller, *J. Chem. Phys.*, 2007, **126**, 124311.
- 10 P. E. Hintze, S. Aloisio and V. Vaida, *Chem. Phys. Lett.*, 2001, **343**, 159–165.
- 11 Z. Xue and M. A. Suhm, *Mol. Phys.*, 2010, **108**, 2279–2288.
- 12 A. D. H. Clague and H. J. Bernstein, *Spectrochim. Acta, Part A*, 1969, **25**, 593–596.
- 13 S. M. Lofgren, P. R. Mahling and J. B. Togeas, *J. Phys. Chem. A*, 2005, **109**, 5430–5437.
- 14 L. Pérez-García and D. B. Amabilino, *Chem. Soc. Rev.*, 2007, **36**, 941–967.
- 15 A. Zehnacker and M. A. Suhm, *Angew. Chem., Int. Ed.*, 2008, **47**, 6970–6992.
- 16 M. Albrecht, A. Borba, K. Le Barbu-Debus, B. Dittrich, R. Fausto, S. Grimme, A. Mahjoub, M. Nedić, U. Schmitt, L. Schrader and M. A. Suhm, *New J. Chem.*, 2010, **34**, 1266–1285.
- 17 S. Tsuzuki, H. Orita, H. Ueki and V. A. Soloshonok, *J. Fluorine Chem.*, 2010, **131**, 461–466.
- 18 D. Usvyat, L. Maschio, C. Pisani and M. Schütz, *Z. Phys. Chem.*, 2010, **224**, 441–454.