

The partitioning of disparlure between hydrophobic organic solvents and water

Sierra Rayne^{a,*}, Kaya Forest^b

^aChemologica Research, 318 Rose Street, PO Box 74, Mortlach, Saskatchewan, Canada, S0H 3E0

^bDepartment of Environmental Engineering, Saskatchewan Institute of Applied Science and Technology, Palliser Campus, 600-6th Avenue NW, PO Box 1420, Moose Jaw, Saskatchewan, Canada, S6H 4R4

Abstract

The partitioning behavior of disparlure ((7R,8S)-*cis*-7,8-epoxy-2-methyloctadecane) - a sex pheromone of the gypsy moth, *Lymantria dispar* - between aqueous solutions and the organic solvents chloroform and n-heptane has been re-evaluated. Prior estimates from the literature of the aqueous-organic solvent partitioning coefficients (log P) for disparlure in these two solvent systems appear to have been underestimated by about 5-6 orders of magnitude. In the current work, we provide corrected log P(chloroform/water) and log P(heptane/water) values for disparlure of 9.87 and 9.15, respectively.

Keywords:

disparlure, (7R,8S)-*cis*-7,8-epoxy-2-methyloctadecane, sex pheromone, gypsy moth, partitioning behavior

Introduction

The partitioning behavior of disparlure ((7R,8S)-*cis*-7,8-epoxy-2-methyloctadecane) - a sex pheromone of the gypsy moth, *Lymantria dispar* - at hydrophobic/aqueous interfaces is of interest to better understand the interaction of this compound with pheromone-binding proteins *in vivo* [1]. In their article, Reimer et al. [1] report the following experimental (expt.) and computationally (calc.) derived chloroform/water and n-heptane/water partitioning coefficients (log P) for disparlure: log P(chloroform/water): 3.4+/-0.3 (expt.), 3.1 (calc.); log P(heptane/water): 3.8+/-0.2 (expt.), 3.9 (calc.).

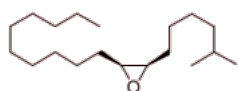


Figure 1: Structure of disparlure.

The SPARC software program (<http://archemcalc.com/sparc/>; October 2011 release w4.6.1691-s4.6.1687) has been validated for accurately estimating the log P values for a wide range of organic compounds [2-4]. This program estimates log P(n-octanol/water), log P(chloroform/water), and log P(heptane/water) for disparlure of 8.24, 9.87, and 9.15, respectively, at 298.15 K. Previous works have also reported estimated log P(n-octanol/water) of about 8 for disparlure using other software [5, 6].

Disparlure is a long chain hydrocarbon with an epoxide moiety near the center of the alkyl chain. A substantial

body of work has established that the difference in partitioning behavior for ether linkages is minimal between aqueous-organic partitioning systems where the organic phase is capable of hydrogen bonding (e.g., n-octanol) and where the organic phase is non-polar (e.g., chloroform, n-heptane, cyclohexane) [7, 8]. Similar results are obtained where the functional group in question is a carbonyl moiety. Consequently, relatively little difference is expected in the log P(n-octanol/water), log P(chloroform/water), and log P(heptane/water) values for disparlure.

To confirm that SPARC is estimating accurate log P values for disparlure, the program was tested with other model compounds relevant to the study in question. For 1,2-epoxybutane, the experimental log P(n-octanol/water) is 0.68 [9], which compares very favorably to the SPARC estimated log P(n-octanol/water) of 0.94, and the SPARC estimated log P(chloroform/water) and log P(heptane/water) values of 1.31 and 0.88, respectively. Similarly, epichlorohydrin has an experimental log P(n-octanol/water) of 0.26 [10], which is in excellent agreement with the SPARC estimated log P(n-octanol/water) of 0.63, and the SPARC estimated log P(chloroform/water) and log P(heptane/water) values of 1.1 and 0.41, respectively.

As well, the environmental contaminant heptachlor epoxide has an experimental log P(n-octanol/water) of 5.40 [11], also in excellent agreement with the SPARC estimated log P(n-octanol/water) of 5.74, and the SPARC estimated log P(chloroform/water) and log P(heptane/water) values of 7.17 and 5.65, respectively. Thus, SPARC appears capable of accurately predicting log P(n-octanol/water) values for a range of epoxides, and consistent with our state-of-the-art knowledge regarding aqueous-organic partitioning behavior between various organic solvents, SP-

*Corresponding author. Tel.: +1 306 690 0573. E-mail address: sierra.rayne@live.co.uk (S. Rayne).

ARC also predicts little difference between the log P(n-octanol/water), log P(chloroform/water), and log P(heptane/water) values for the various epoxides.

Because of the polarity of the epoxy moiety, the log P value of an alkane will be reduced by introduction of such a functionality. As already noted above, 1,2-epoxybutane has an experimental log P(n-octanol/water) of 0.68. The corresponding alkane (n-butane) has an experimental log P(n-octanol/water) of 2.89, in excellent agreement with the SPARC estimated log P(n-octanol/water) of 2.72, and the SPARC estimated log P(chloroform/water) and log P(heptane/water) values of 3.14 and 3.32, respectively. The non-epoxylated analog of disparlure is 2-methyloctadecane, which has SPARC estimated log P(n-octanol/water), log P(chloroform/water), and log P(heptane/water) of 11.22, 12.70, and 13.17, respectively. Thus, if we assume about a 2-3 log unit reduction in the log P of an alkane upon introduction of an epoxide moiety, disparlure would be expected to have log P values of about 8-10 in the various solvents under consideration, which is also in excellent agreement with the SPARC direct log P prediction for disparlure discussed above. Finally, Reimer et al. [1] quote an experimental log P(chloroform/water) of 6.57 for n-nonane, in excellent agreement with the SPARC log P(chloroform/water) estimate for this compound of 6.28 (of note, SPARC also predicts log P(n-octanol/water) and log P(heptane/water) of 5.47 and 6.49, respectively, for n-nonane).

Consequently, there is no reason to believe that the SPARC log P(chloroform/water) and log P(heptane/water) estimates (as well as prior log P estimates in the literature) for disparlure are not correct. It therefore appears that Reimer et al. [1] have underestimated the log P(chloroform/water) and log P(heptane/water) for disparlure by about 5-6 orders of magnitude. The source of the discrepancy is unknown. If hydrolysis of the epoxide in disparlure had occurred during the experimental trials in ref. [1], this would still yield a highly hydrophobic (SPARC log P(chloroform/water)=8.19) long-chain alkane with a secondary alcohol near the center of the chain, which could not explain the very low experimental log P(chloroform/water) for disparlure reported in ref. [1]. The authors in ref. [1] also state that “[t]he agreement between the experimental and calculated values validates the choice of the force field parameters, which can thus be used in future MD [molecular dynamics] simulations of the PBP-pheromone interactions.” Until the source of the large discrepancies in log P values for disparlure highlighted above are resolved by these authors, confidence in their force field parameters should be considered low.

References

[1] S. Reimer, C. Van Klei, Y. Yu, E. Plettner, N. Weinberg, Partition coefficients of disparlure at hydrophobic/aqueous interfaces: A comparative experimental and theoretical study, *Canadian Journal of Chemistry* 89 (2011) 568–572.

[2] S. Hilal, L. Carreira, S. Karickhoff, Prediction of the solubility, activity coefficient, gas/liquid and liquid/liquid distribution coefficients of organic compounds, *QSAR & Combinatorial Science* 23 (2004) 709–720.

[3] S. Rayne, K. Forest, Perfluoroalkyl sulfonic and carboxylic acids: A critical review of physicochemical properties, levels and patterns in waters and waste waters, and treatment methods, *Journal of Environmental Science and Health, Part A: Toxic / Hazardous Substances and Environmental Engineering* 44 (2009) 1145–1199.

[4] S. Rayne, K. Forest, Dow and Kaw,eff vs. Kow and K^{ow}: Acid/base ionization effects on partitioning properties and screening commercial chemicals for long-range transport and bioaccumulation potential, *Journal of Environmental Science and Health, Part A: Toxic/Hazardous Substances and Environmental Engineering* 45 (2010) 1550–1594.

[5] P. Durkin, Control/Eradication Agents for the Gypsy Moth - Human Health and Ecological Risk Assessment for Disparlure (a.i.) and Disrupt II Formulation, United States Department of Agriculture: Atlanta, GA, USA, 2006.

[6] A. Herrmann, *The Chemistry and Biology of Volatiles*, John Wiley and Sons, Ltd: Chichester, UK, 2010, 2010, Ch. Volatiles - An interdisciplinary approach.

[7] C. Chiou, *Partition and Adsorption of Organic Contaminants in Environmental Systems*, John Wiley and Sons: New York, USA, 2002.

[8] R. Todeschini, V. Consonni, R. Mannhold, *Molecular Descriptors for Chemoinformatics*, Wiley-VCH: New York, USA, 2009.

[9] OECD, *Screening Information Dataset Report for 1,2-Epoxybutane*, Organisation for Economic Co-operation and Development: Paris, France, 2001.

[10] USEPA, *Technical Factsheet on Epichlorohydrin*, United States Environmental Protection Agency: Washington, DC, USA, 2011.

[11] Syracuse Research Corporation, *Toxicological Profile for Heptachlor and Heptachlor Epoxide*, Agency for Toxic Substances and Disease Registry, Public Health Service, United States Department of Health and Human Services: Atlanta, GA, 2007.