J Therm Anal Calorim (2010) 99:71–73
DOI 10.1007/s10973-009-0455-z

Ab initio and DFT calculations of three-body interactions in chiral mixtures

M. Fujisawa · T. Kimura

Japan Symposium 2008

Abstract In order to elucidate the enthalpic stabilization of a 2-methyl-1,4-butanediol system (2M14BD) and a 3-chloro-1,2-propanediol (3C12PDO) system by mixing of each (*R*)- and (*S*)-enantiomers, three-body interaction energies are obtained by PW91/6-311G** and MP2/6-311G** level calculations. The differences between homochiral interactions and heterochiral interactions in a 3C12PDO system are found. On the other hand, in 2M14BD systems, very slight differences can be observed between the three-body interaction energies of the three ternary systems. Further, the relationship between excess enthalpies and chiral interactions is discussed.

Keywords Excess enthalpy · Chiral interaction · Three-body interaction · Ab initio molecular orbital method

Introduction

Elucidating the role of asymmetric intermolecular interactions occurring due to stereo-specific structures of a molecule is very important for understanding the mechanisms of reactions in chemistry and biochemistry. In particular, stereospecific interactions due to neighboring surfaces may play a major role in, for examples, enzyme–substance reactions, antigen–antibody reactions, certain kinds of mechanisms of the senses of smell and taste, etc. In 1966, Takagi et al. [1] found that small enthalpies of mixing of two enantiomers of some compounds were measurable by microcalorimetry. Later, Atik et al. [2, 3] also studied other optical isomers by microcalorimetry. Recently, the thermal properties of D-amino acids were studied [4–6]. In our previous article [7–9], enthalpies of mixing of more than 20 systems of (*R*)- and (*S*)-enantiomers were reported. All measured systems showed a very small enthalpy change. Mixing of enthalpies of most heterochiral liquids systems caused enthalpic destabilization over the entire range of mole fractions, except for numerical systems. For example, mixing of hetero-chiral liquids 3-chloro-1,2-propanediol (3C12PDO) caused enthalpic destabilization, whereas that of 2-methyl-1,4-butanediol (2M14BDO) caused enthalpic stabilization, as observed in Table 1. It is possible to form an intermolecular hydrogen bond in these systems. For example, a 2M14BDO molecule can form an intra-molecular hydrogen bond, though the probability of such bond formation is very small. In this study, to elucidate the relationship between excess enthalpies and chiral interactions, we perform ab initio molecular orbital calculations and density functional theory (DFT) calculations.

Computational method

To study molecular interactions occurring in chiral mixtures, ab initio calculations were performed using the Gaussian 03 program [10]. Electron correlation was accounted for the DFT and second-order Møller–Plesset perturbation (MP2) level. The geometries of monomers ((*R*)-3C12PDO, (*S*)-3C12PDO, (*R*)-2M14BD, and (*S*)-2M14BD) were optimized at the Perdew and Wang's 1991 gradient-corrected correlation functionals

M. Fujisawa (✉)
Department of Biotechnological Science, Kinki University,
930 Nishimitani, Kinokawa-City, Wakayama 649-6493, Japan
e-mail: fujisawa@waka.kindai.ac.jp

T. Kimura
Department of Chemistry, Kinki University, Kowakae,
Higashi-osaka 577-8502, Japan

Table 1 Excess enthalpies of equimolar mixtures of the two enantiomers

System	H^E ($x = 0.5$)/J mol^{-1}
3-Chloro-1,2-propanediol	22.54 [5]
2-Methyl-1,4-butanediol	−2.25 [5]

(PW91)/6-311G** level. The geometries of three ternary systems ((1) (*R*)-form + (*R*)-form + (*R*)-form, (2) (*R*)-form + (*R*)-form + (*S*)-form, and (3) (*R*)-form + (*S*)-form + (*S*)-form) were also optimized at the PW91/6-311G** level. The PW91 method is a cooperatively better method for estimating the hydrogen bond [11]. The center of gravity of each optimized enantiomers was arranged on top of equilateral triangles. Each enantiomer was arranged in various directions, while maintaining the position of its center of gravity. These structures were decided to the initial structure of optimization of the ternary systems. The geometries of complexes were optimized from several initial geometries. All single point energy calculations were performed by the molecular orbital method by using the SCF = tight option. The total interaction energies were corrected using the basis set superposition error (BSSE).

Results and discussion

Examples of optimized geometries of 3C12PDO ternary systems ((*R*) + (*S*) + (*S*)) are shown in Fig. 1a, b. It appears that the complex **1a** forms three intermolecular hydrogen bonds, for the first bond, the O–H distance is 0.09472 nm, the H···O distance is 0.20349 nm, and the O–H···O angle is 151.150°; for second bond, the O–H distance is 0.09441 nm, the H···O distance is 0.20651 nm, and the O–H···O angle is 172.514°; for the third bond, the O–H distance is 0.09469 nm, the H···O distance is 0.20722 nm, and the O–H···O angle is 153.565°. Similarly, the complex **1b** appears to form two intermolecular hydrogen bonds, for the first bond, the O–H distance is 0.09440 nm, the H···O distance is 0.20980 nm, and the O–H···O angle is 171.555°, and for the second bond, the O–H distance is 0.09471 nm, the H···O distance is 0.20069 nm, and the O–H···O angle is 152.109°. An example of optimized geometries of 2M14BDO ternary systems ((*R*) + (*R*) + (*R*)) is shown in Fig. 2. As shown in this figure, 2M14BDO ternary systems ((*R*) + (*R*) + (*R*)) also form intermolecular hydrogen bonds. However, they do not appear to form intramolecular hydrogen bonds.

The molecular interaction energies of binary systems are calculated as follows:

$$\Delta E(\mathrm{AB}) = E(\mathrm{AB}) - E(\mathrm{A}) - E(\mathrm{B}). \qquad (1)$$

It should be noted that additional hydrogen bonds are formed together with already existing hydrogen bonds. Further, an attempt is made to determine the cooperative increment of three-body interactions [12–17] of the following two systems.

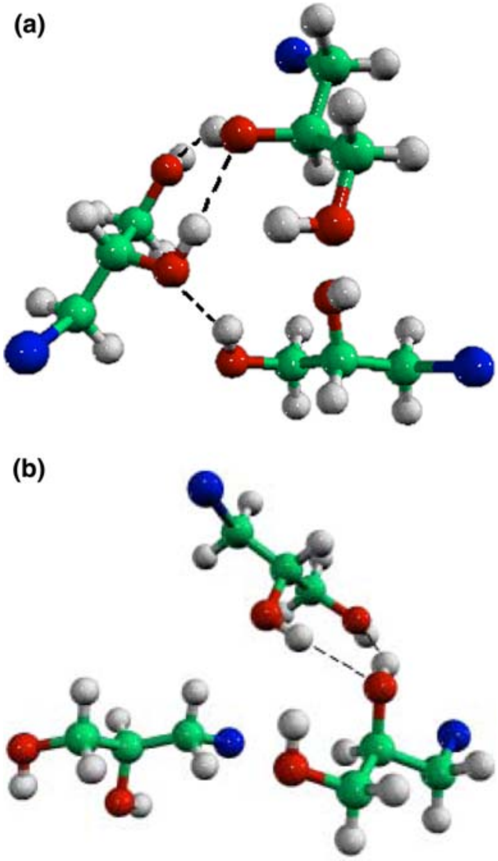

Fig. 1 **a** Example of optimized geometries of the complex of ((*R*)-3C12PDO + (*S*)-3C12PDO + (*S*)-3C12PDO). **b** Example of optimized geometries of the complex of ((*R*)-3C12PDO + (*S*)-3C12PDO + (*S*)-3C12PDO)

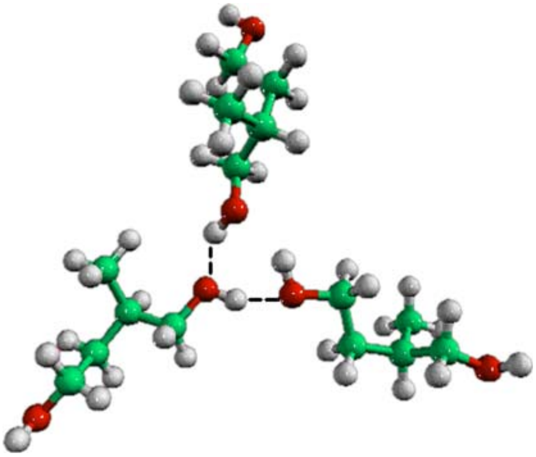

Fig. 2 Example of optimized geometries of the complex of ((*R*)-2M14BDO + (*R*)-2M14BDO + (*R*)-2M14BDO)

Table 2 Average values of three-body interaction energies for the ternary systems of enantiomers

System	$\Delta_{\mathrm{tern}}E_{\mathrm{coop}}$/kJ mol^{-1} (MP2)	$\Delta_{\mathrm{tern}}E_{\mathrm{coop}}$/kJ mol^{-1} (PW91)
(*R*)-3C12PDO + (*R*)-3C12PDO + (*R*)-3C12PDO[a]	−29.8	−24.0
(*R*)-3C12PDO + (*R*)-3C12PDO + (*S*)-3C12PDO	−25.3	−19.7
(*R*)-3C12PDO + (*S*)-3C12PDO + (*S*)-3C12PDO	−26.6	−20.9
(*R*)-2M14BDO + (*R*)-2M14BDO + (*R*)-2M14BDO[b]	−26.3	−20.4
(*R*)-2M14BDO + (*R*)-2M14BDO + (*S*)-2M14BDO	−26.9	−21.1
(*R*)-2M14BDO + (*S*)-2M14BDO + (*S*)-2M14BDO	−26.1	−20.0

[a] 3-Chloro-1,2-propanediol

[b] 2-Methyl-1,4-butanediol

Three-body interaction energies of A–B–C complex systems are calculated using fixed structures that optimized ternary systems, as follows:

$$\begin{aligned}
\Delta_{\mathrm{tot}}E_{\mathrm{coop}} &= {}_{\mathrm{ABC}}E_{\mathrm{ABC}} - ({}_{\mathrm{ABC}}E_{\mathrm{A}} + {}_{\mathrm{ABC}}E_{\mathrm{B}} + {}_{\mathrm{ABC}}E_{\mathrm{C}}),\\
\Delta_{\mathrm{bin}}E_{\mathrm{coop}} &= {}_{\mathrm{ABC}}E_{\mathrm{AB}} - ({}_{\mathrm{ABC}}E_{\mathrm{A}} + {}_{\mathrm{ABC}}E_{\mathrm{B}}) + {}_{\mathrm{ABC}}E_{\mathrm{AC}}\\
&\quad - ({}_{\mathrm{ABC}}E_{\mathrm{A}} + {}_{\mathrm{ABC}}E_{\mathrm{C}}) + {}_{\mathrm{ABC}}E_{\mathrm{BC}}, - ({}_{\mathrm{ABC}}E_{\mathrm{B}} + {}_{\mathrm{ABC}}E_{\mathrm{C}}),\\
\Delta_{\mathrm{tern}}E_{\mathrm{coop}} &= \Delta_{\mathrm{tot}}E_{\mathrm{coop}} - \Delta_{\mathrm{bin}}E_{\mathrm{coop}}, \qquad (2)
\end{aligned}$$

where subscripts tot, coop, bin, and tern denote total, cooperative, binary, and ternary, respectively, and ${}_{X}E_{Y}$ is an energy system of extracted fixed structure Y from structure that optimized ternary complex X. Average values of the three-body interaction energies of the ternary systems of enantiomers are listed in Table 2.

In 3C12PDO systems that show enthalpic destabilization, the three-body interaction energies $\Delta_{\mathrm{tern}}E_{\mathrm{coop}}$ of ((*R*) + (*R*) + (*R*)) is 10% more larger than those of ((*R*) + (*R*) + (*S*)) and ((*R*) + (*S*) + (*S*)). Therefore, this situation indicates that 3C12PDO systems became non-random mixing. On the other hand, in 2M14BD systems that are almost athermal, very slight differences can be observed between the three-body interaction energies of the three ternary systems. Thus, the differences between homochiral interactions and heterochiral interactions correspond to excess enthalpies of mixing of the enantiomers. Therefore, the relationship between excess enthalpies and chiral interactions is proved by the molecular orbital method.

References

1. Takagi S, Fujishiro R, Amaya M. Heats of mixing of optical isomers in solution: calorimetric evidence of stereospecific effect. J Chem Soc Chem Commun. 1968;10:480.
2. Atik Z, Ewing MB, McGlashan ML. Chiral discrimination in liquids. Excess molar volumes of (1−x)A++xA−, where A denotes limonene, fenchone, and α-methylbenzylamine. J Phys Chem. 1981;85:3300–3.
3. Atik Z, Ewing MB, McGlashan ML. Chiral discrimination in liquids II. Excess molar enthalpies of {(1−x)A++xA−}, where A denotes fenchone or α-methylbenzylamine. J Chem Thermodyn. 1983;15:159–63.
4. Fujisawa M, Matsushita T, Khan MA, Kimura T. Excess molar heat capacities of (L-glutamine aqueous solution + D-glutamine aqueous solution) at temperatures between 293.15 and 303.15 K. J Therm Anal Cal. 2005;82(2):319–21.
5. Matthews ME, Atkinson I, Presswala L, Najjar O, Gerhardsteiny N, Wei R, et al. Dielectric classification of d-and l-amino acids by thermal and analytical methods. J Therm Anal Cal. 2008;93(1): 281–7.
6. Presswala L, Matthews ME, Atkinson I, Najjar O, Gerhardstein N, Moran J, et al. Discovery of bound and unbound waters in crystalline amino acids revealed by thermal analysis. J Therm Anal Cal. 2008;93(1):295–300.
7. Kimura T, Matsushita T, Ueda K, Aktar F, Matsuda T, Kamiyama T, et al. Enthalpic changes on mixing two couples of S- and R-enantiomers of heptane-2-ol, octane-2-ol, nonane-2-ol, 3-chloro-propane-1,2-diol, 2-methyl-1,4-butanediol at 298.15 K. Thermochica Acta. 2004;414:209–14.
8. Kimura T, Khan MA, Ishii M, Ueda K, Matsushita T, Kamiyama T, et al. Enthalpic changes on mixing two couples of S- and R-enantiomers of benzyl-(1-phenyl-ethyl)-amine, 1-phenylethyl-amine, 1-phenyl-ethanol, butyric acid oxiranylmethyl ester, 4-methyl-[1,3]dioxolan-2-one, 2-chloro-methyloxirane and 3-hydroxy-isobutyric acid methyl ester at T=298.15 K. J Chem Thermodyn. 2006;38(8):1042–8.
9. Kimura MAK, Kamiyama T. Enthalpies of mixing and apparent molar volumes of ethanol solution of chiral dicarboxylic acids. J Therm Anal Cal. 2006;85(3):559–65.
10. Frisch MJ et al. Gaussian 03, revision D.01, user's reference manual. 2nd ed. Wallingford, CT: Gaussian, Inc.; 2005.
11. Tsuzuki S, Hujou H, Nagawa Y, Goto M, Hiratani K. Cooperative enhancement of water binding to crownophane by multiple hydrogen bonds: analysis by high level ab initio calculations. J Am Chem Soc. 2001;123:4255–8.
12. Mierzwicki K, Latajka Z. Basis set superposition error in N-body clusters. Chem Phys Lett. 2003;380:654–64.
13. Solimannejad M, Alkorta I, Elguero J. A computational study of dimers and trimers of hypohalous acids. Chem Phys Lett. 2008;454:201–6.
14. Mayer I, Vibók Á, Halász G, Valiron P. A BSSE-free SCF algorithm for intermolecular interactions. 111. Generalization for three-body systems and for using bond functions. Int J Quantum Chem. 1998;57(5):1049–55.
15. Parra RD, Zeng XC. Hydrogen bonding and cooperative effects in mixed dimers and trimers of methanol and trifluoromethanol: an ab initio study. J Chem Phys. 1999;110:6329–38.
16. Masella M, Greshb N, Flament J-P. A theoretical study of non-additive effects in four water tetramers. J Chem Soc Faraday Trans. 1998;94:2745–53.
17. Li X, Liang J. Geometric cooperativity and anticooperativity of three-body interactions in native proteins. Proteins. 2005; 60: 46–65.