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Chirality Transfer Mechanism for Optical D/L Lactic Acid Isomers: A theoretical Study Based on the Scaled Hypersphere Search Method

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Lactic acid is chiral and has two optical isomers. One is known as L-(+)-lactic acid or (*S*)-lactic acid and the other, its mirror image, is D-(-)-lactic acid or (*R*)-lactic acid. L-(+)-Lactic acid is the biologically important isomer. Molecular chirality is one of the fundamental characteristics of molecules, and it plays an important role in stereochemistry and biochemisty. Specifically, the homo-chirality of biological molecules (the use of only left-handed L-configuration amino acids and only right-handed D-configuration sugars) has long been known to be an important characteristic of life. Notable problems endure regarding the molecular evolution, which culminated in the homo-chiral biopolymers associated with contemporary terrestrial life. How was Nature's selection of these stereochemical structures, a random one, or were determinate processes involved? All these questions urged us to investigate their reaction pathways on potential energy surface (PES), which is a fascinating research goal.

The Scaled hypersphere search (SHS) method [1-3] makes it possible to explore unknown reaction pathways on PES. This method enables us to make a global analysis of the potential energy surface by detecting the anharmonic downward distortions of PES as energy minima on a hyper surface which would have a constant energy if the potentials are harmonic. In this study, intramolecular D-L conversion pathways of lactic acid have been discovered by the application of the SHS method to exploring potential energy surfaces at the level of HF/6-31G based on a Gaussian03 program package. From each TS, downhill techniques toward both sides were carried out to determine the minimum energy path or the intrinsic reaction coordinate (IRC).

Fig.1 shows D-L conversion pathways between optical isomers of lactic acid. Starting from one of the most stable isomer with point chirality, reaction pathways leading to neighboring transition state were searched systematically from its equilibrium structure. As can be seen in Fig.1, four conversion channels, (A), (B), (C), and (D), were discovered between D and L lactic acid. No direct conversion channel via only one TS exists between D and L isomers of lactic acid.

Channel (a) includes two types of dissociated achiral intermediate states with Cs symmetry that are of hydrogen-bond characters. Similar to the channel (C) in D-L conversion of Alanine [4], Channel (b) surmounts a chiral transition state to descend to an intermediate with axial chirality, which is then transformed to its counterpart with the opposite chirality via an achiral transition state with Cs symmetry. Channel (c) and (d) show processes from the lactic acid to another two intermediates via the cleavage of C-O bond and the formation of H_2O. Actually, Channel (c) is a pathway via a chiral transition state into an intermediate with helical chirality, while Channel (d) is a process via an intermediate with axial chirality, corresponding to channel (B) and (D) in D-L conversion of Alanine [4], respectively. The present results show channel (a) in this study is a newly found pathway.

Since the first transition state in every channel has a high barrier larger than 200 kJ/mol, lactic acid molecule is kinetically stable enough to keep its own chirality under thermally mild conditions. The

preference of D-L conversion routes is expected as (a)>(b)>(c)>(d) from the magnitudes of the barrier heights of respective transition state. Since the inter-conversion of four functional groups around the asymmetric carbon atom (C*) can be summarized into a combination of two functional groups, which can rotate to its counterpart to yield the other optical isomer with the opposite chirality, as shown in Ref. [4], in this study, the rotation of four couple of functional groups around the asymmetric carbon atom of lactic acid, (OH, COOH), (H, COOH), (H, OH), and (CH_3, COOH) are allowed for the D-L conversion channels of (a), (b), (c), and (d), respectively.

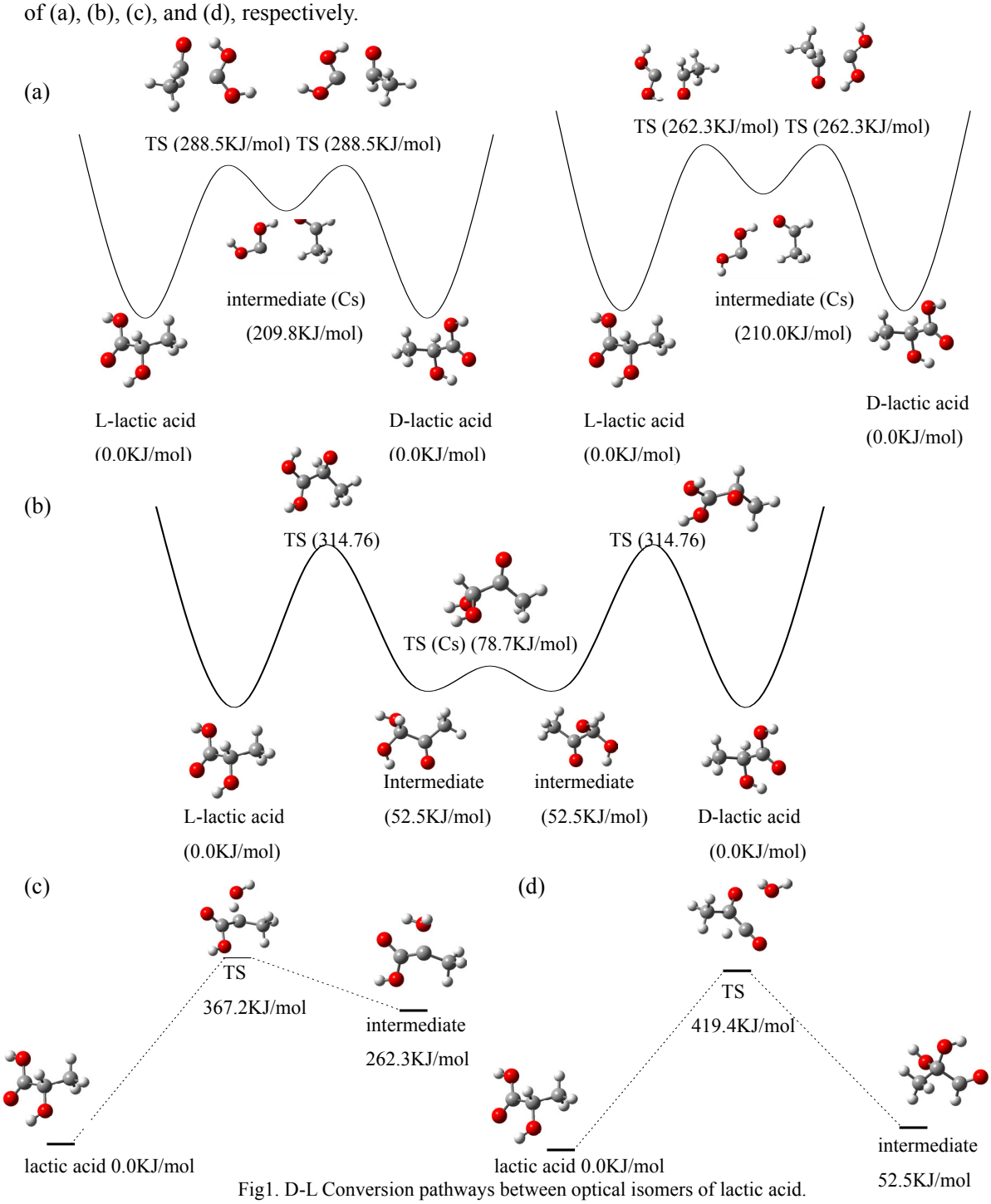

Fig1. D-L Conversion pathways between optical isomers of lactic acid.

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