Solvent Effect and Molecular Orbital Study on the Specific Rotation of a Methacrylamide Having L-Leucine Structure in the Side Chain

Fumio Sanda, Masafumi Nakamura, and Takeshi Endo*

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta-cho, Midori-ku, Yokohama 226

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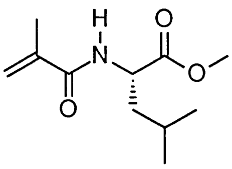
Solvent effect and molecular orbital studies on the specific rotation of a methacrylamide (MA-(L)-L-M) having L-leucine structure in the side chain were carried out. The larger the relative dielectric constant of the solvent, the more stable the conformation of MA-(L)-L-M showing larger polarity was. This conformation change depending on the solvent might be the reason for the solvent effect on the specific rotation of MA-(L)-L-M.

Various vinyl monomers having α-amino acid moieties have been reported.[1] Unique polymerization behavior, structure, and properties of the polymers based on chirality are expected. L-Leucine, one of the essential amino acids, has a strong hydrophobic nature based on its isobutyl group, and it plays an important role in α-helix formation and stabilization of peptides and proteins.[2] Poly(L-leucine) can form the α-helix by itself[3] and therefore, it has been examined as a biocompatible material such as an artificial skin[4] and fiber.[5] We have developed amino acids and peptides as biocompatible materials as well as optical and chemical functional materials.[6] Recently, we have reported synthesis and radical polymerization of a methacrylamide having L-leucine methyl ester structure, *N*-methacryloyl-L-leucine methyl ester (MA-(L)-L-M).[7] Radical polymerization behavior of MA-(L)-L-M was unique and interesting. Namely, the monomer reactivity ratio of MA-(L)-L-M was larger than that of methyl methacrylate differently from usual methacrylamides. Moreover, both inversion and increase of absolute value of specific rotation in the transformation from MA-(L)-L-M (+1.3°) to poly(MA-(L)-L-M) (-35.7°) could be observed. In this paper, solvent effect on the specific rotation of MA-(L)-L-M was examined, and analyzed by molecular orbital (MO) calculation.

Specific rotations ($[\alpha]_D$) were measured at 25 °C on a JASCO DIP-1000 digital polarimeter using sodium lamp as a light source. All MO computations were done on an Apple Power Macintosh 7100/80$_{AV}$, equipped with a 40 MHz CXP coprocessor-board with use of SONY Tektronix CAChe system version 3.7. The initial geometry was obtained from the single crystal X-ray analytical data. The Geometry was fully optimized for all geometrical variables (bond lengths, bond angles, and dihedral angles) using PM3 Hamiltonian by restricted Hartree-Fock method and the Conductor-like Screening Model (COSMO).[8]



MA-(L)-L-M

Figure 1 illustrates the relationships between the specific rotation measured in various solvents and calculated heat of formation of MA-(L)-L-M in the solvent *vs* relative dielectric constant of the solvent. The larger the dielectric constant of the measuring solvent, the negatively larger the $[\alpha]_D$ of MA-(L)-L-M in the solvent was. The relationship between the dielectric constant of the solvent and the heat of formation calculated by MO COSMO method well agreed with that between the dielectric constant and $[\alpha]_D$ of MA-(L)-L-M. Figure 2 illustrates the relationship between the dihedral angle Ψ, Cα-Cβ-N-Cγ, and dipole moment of MA-(L)-L-M *vs* relative dielectric constant of the solvent. MA-(L)-L-

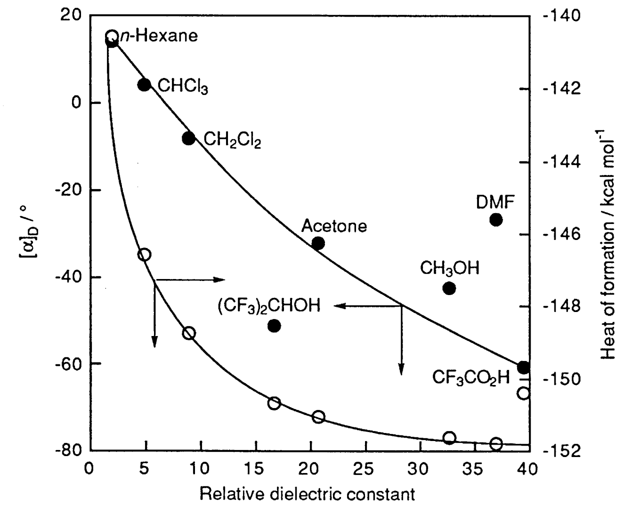


Figure 1. Specific rotation and calculated heat of formation of MA-(L)-L-M *vs* relative dielectric constant of the solvent.

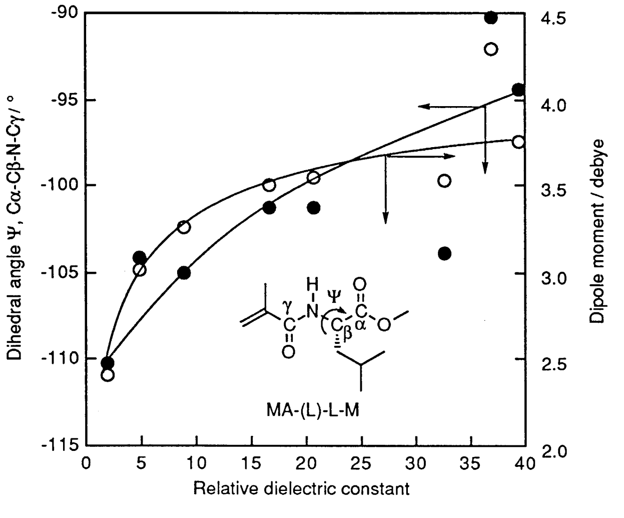


Figure 2. Dihedral angle Ψ, Cα-Cβ-N-Cγ and dipole moment of MA-(L)-L-M *vs* relative dielectric constant of the solvent.

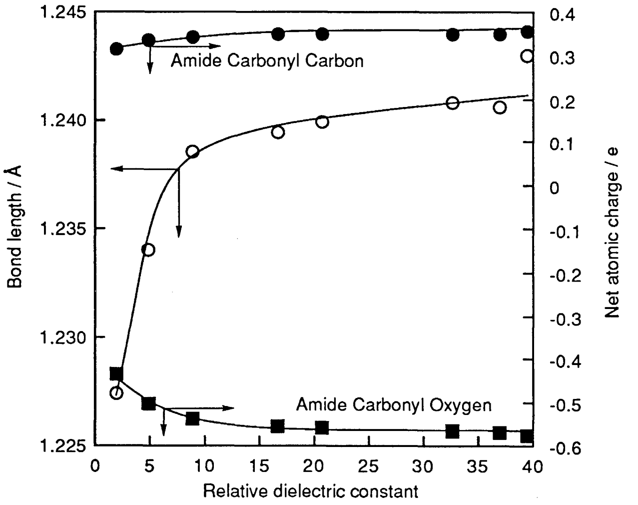


Figure 3. Bond length and net atomic charge of amide carbonyl group of MA-(L)-L-M *vs* relative dielectric constant of the solvent.

M changes its conformation according to the polarity of the solvent. Namely, the larger the dielectric constant, the positively larger the dihedral angle Ψ becomes to increase the dipole moment of the molecule.[9] Moreover, the bond length of the amide carbonyl group and net atomic charges of the carbon and oxygen of the amide carbonyl group of MA-(L)-L-M also change to increase the polarity of the molecule with increase of the polarity of the solvent (Figure 3).

In summary, solvent effect on the specific rotation of MA-(L)-L-M was examined, and molecular orbital study concerning the solvent effect was carried out. It was suggested that the conformation of MA-(L)-L-M changed to show larger polarity with increase of the polarity of the solvent. This may be the first attempt to examine the specific rotation of an optically active compound by MO calculation.

References and Notes

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9 The deviation of $[\alpha]_D$, ψ, and dipole moment values in polar solvents such as $(CF_3)_2CHOH$, CH_3OH, and DMF may come from the effect of hydrogen bonding between MA-(L)-L-M and the solvents, since the COSMO method does not take into account hydrogen bonding directly. Hydrogen bonding as well as relative dielectric constant should considerably affect the conformation of MA-(L)-L-M.