1. **No.**

   FP01801013

2. **Title**

   Synthetic Studies of DNA adducts and their amidites for DNA adductome analysis

3. **Period**

   2017-2019

4. **Summary**

   Lipid peroxidation products, such as 4-oxo-2-hexenal (OHE) and 4-oxo-2-nonenal (ONE), directly react with DNA and produce various exocyclic etheno-base DNA adducts, some of which are considered to contribute to carcinogenesis. However, the system for repairing them in humans is almost unknown.

   The lipid peroxidation products (OHE and ONE) were synthesized successfully from 2-substituted furans. And the reaction of 2'-deoxyribonucleosides (dC and dG) with OHE and ONE were efficiently carried out on a large-scale than reported performing the conjugate addition-cyclization to afford DNA adducts. Thus obtained DNA-adducts were transformed to the corresponding amidites. However, the reaction of 2'-deoxyadenosine (dA) and its derivatives with OHE (or ONE) were not effectively realized. For the preparation of DNA-adducts about dA, α-bromo-γ-ketoaldehyde derivatives, which are equivalent to lipid peroxidation products, were designed and their synthetic studies were carried out.

   Additionally, other adducts, such as ethylated-base DNA adducts (N3 - O4 -, O2 -ethyl-dT) were also synthesized by the reaction with diazoethane-ether solution.