

LABORATORY OF PLANT PRODUCT CHEMISTRY

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The Laboratory of Plant Product Chemistry was established by the late Dr. M. Ohno in 1957 to pursue research on the chemistry of biologically active organic substances of plant origin and the related compounds. Along this line, 4 permanent staffs, Professor Dr. Y. Inouye, Associate Professor Dr. J. Oda, Dr. N. Baba, and Mr. Y. Yamamoto have been working in collaboration with 4 operators and 5 graduate students. During the last decade, 8 research associates, 10 operators and 16 graduate students have joined the laboratory and contributed very much to the activities: 14 M. S. and 9 Ph.D. degrees have been granted on research works performed in this laboratory.

Experimental facilities and equipments involve modern instruments such as UV-, IR-, ORD-, and NMR-spectrometers and gas-chromatographs for qualitative and preparative purposes in addition to the conventional apparatuses.

Phytochemical studies of pyrethrum and leaf alcohol which were the main subject in the postwar time, have been worked out and been phased out since earlier 1960's, except pyrethroid assay by means of spectrophotometry and gas-chromatography.

Research interest has then been focused on stereochemistry, in particular on asymmetric synthesis. Asymmetric inductions in methoxymercuration of α,β -unsaturated esters, the Simmons-Smith reactions, chiral enamines, phosphorus- and sulfur-ylids have been exploited and developed, and the mechanisms heretofore unknown have been thoroughly elucidated by virtue of the stereochemical outcome in respective chiral system.

Of many achievements, the solvent effect in asymmetric synthesis is worthy of note. In a base-catalyzed Michael type cyclopropanation, it was found that the solvent polarity has a marked effect on the stereoselectivity of the reaction *e.g.* changing the solvent medium from toluene to DMF or to nitrobenzene resulted in a complete reversal of sign of optical rotation of the resulting chiral cyclopropane product. In order to elucidate the dynamic stereochemistry unequivocally, asymmetric syntheses of the same type to give 1,2-dimethylcyclopropane-1,2-dicarboxylic acids were designed and conducted in binary solvent systems of continuously varying dielectric constant, consisting of benzene and DMF in volume ratio from 10 : 0 through 0 : 10. The stereochemical results obtained in this system unambiguously showed the solvent polarity-dependence of stereoselectivity of both *cis*, *trans*-steric course and asymmetric induction of the *trans*-acid. Furthermore, when the logarithms of the ratios *cis/trans* and *trans*-(*R* : *R*)/(*S* : *S*) were plotted against the Kirkwood-Onsager parameter, linear relationships were obtained. This finding shows that the solvent effect is correlated fairly well in quantitative terms by Kirkwood-Onsager theory and accordingly has a reasonable theoretical basis. The stereochemical outcome was successfully interpreted also in terms of the electrostatic stabilization by solvation and the non-bonded interactions of

the postulated transition intermediate carbanion conformations with different dipole moments; these conform to the stereoelectronic requirements for orbital overlap and charge delocalization in the rate- and therefore stereochemical-determining cyclization step. After our finding, the same solvent effect has been successively observed in many other asymmetric systems as well, and is now accepted as a rather fundamental phenomenon in general asymmetric synthesis, together with the catalyst, temperature and pressure effects.

Self-immolative asymmetric synthesis is another contribution from our laboratory. Asymmetric inductions in [2,3] and [3,3]sigmatropic rearrangements of chiral allylic amine oxides and trichloroacetimidates were achieved for the first time, in which the chirality originally residing on tetrahedral nitrogen or carbon were successfully transferred to trigonal carbon at the expense of the former in nearly complete retention of chirality. The stereochemical outcome in the designed systems, having been buttressed by the Woodward-Hoffmann rule of conservation of orbital symmetry, enabled us to formulate with certainty the transition state topology for the present chiral systems. This series of studies added to our knowledge of the stereochemistry of this interesting family of rearrangements.

A fundamental theory was proposed for asymmetric double induction as evidenced by the quantitative treatments of optical yields in asymmetric synthesis of cyclopropanes. This also argues against the validity of many "steric models" hitherto proposed for asymmetric systems.

Accumulated knowledge of asymmetric synthesis and the ever-growing interest in bio-organic chemistry prompted us to undertake a study of biomimetic synthesis and some achievements have been obtained in asymmetric reduction of α -ketoesters, quinolinium and iminium salts by the use of chiral 1,4-dihydropyridine derivatives as NAD(P)H model compound.

Our team has been active also in synthetic organic chemistry too. In connection with asymmetric Simmons-Smith reactions, an important modification of the original synthetic procedure was made and has now been widely used for preparing the otherwise difficultly accessible cyclopropanes in good yields.

Exploratory works have been made aiming at a possible synthetic utility of chloramines, in which reactions of chloramines with substituted malonate carbanions, β -diketones, β -ketoesters and enamines were investigated and the mechanisms were elucidated for further applications.

Publications

(* indicates an article published in Japanese)

I. Asymmetric Synthesis

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