Kumamoto University

Study of the Synthesis of New Complex Organic Heterocycles Using Oxidative Radical Reaction, Aerobic Oxidation, Lewis Acid-Catalyzed Reaction, and Photo-Induced Reaction

key words: oxidation, radicals, cyclization, heterocycles, bond-formation, catalytic reaction, photoreaction, aerobic oxidation, peroxides, Lewis acid

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Synthesis of Heterocyclic Propellanes (Figure 1)
Propellanes are containing a tricyclic system connected by a carbon-carbon single bond and of significant theoretical interest as well as biologically important basic scaffold. Efforts are currently underway to synthesize functionalized heterocyclic propellanes using Mn(III)-based oxidative radical tandem cyclization.

Construction of Polyquinane Structure (Figure 2)
Oxidation of a mixture of terminal alkadienes and malonic acid with $Mn(OAc)_3$ gives polyquinane derivatives *via* tandem cyclization. Polyquinane structure is important for total synthesis of natural products and the synthesis of heterocyclic polyquinanes is currently in progress.

Synthesis of Macrocyclic Compounds Using Mn(III)-Based Dihydrofuran-Clipping Reaction (Figure 3)
Electrophilic carbon radicals, produced by the oxidation of carbonyl compounds with metal oxidants, inter- and intra-molecularly attack electron-rich organic molecules to give various cyclic products. Allyloxyoligomethylene 3-oxobutanoates undergo Mn(III)-based dihydrofuran-clipping reaction to give macrocyclic compounds from 11- to 100-members including cyclophene-type huge molecules. Efforts are currently underway to synthesize macrocyclic compounds having various supramolecular behaviors.

Synthesis of Heterocyclic Compounds Including Peroxides and Alkalids (Figure 4)
The biological activity derives from the peroxide structure. The Mn(III)-based oxidative radical reaction of many 1,3-dicarbonyls gives organic peroxides and we synthesized many nitrogen- and oxygen-heterocycle-fused peroxides. We demonstrated that some synthesized peroxides had cytotoxicity and somewhat antimalarial activity. Further studies on the synthesis of more complicated nitrogen-containing bicyclo- and tricycloperoxides using Mn(III)-based oxidation are now in progress.

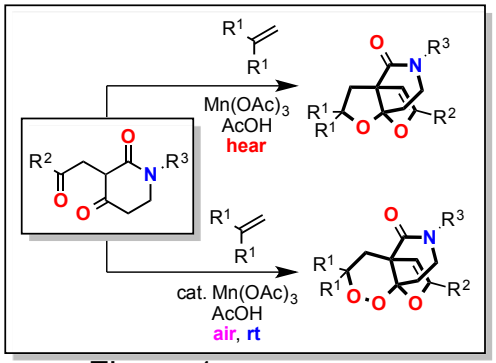

Figure 1

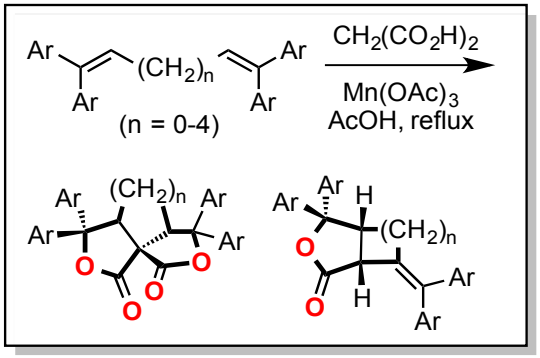

Figure 2

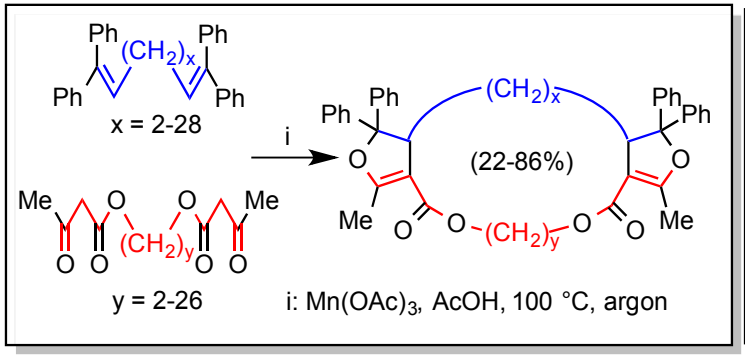

Figure 3

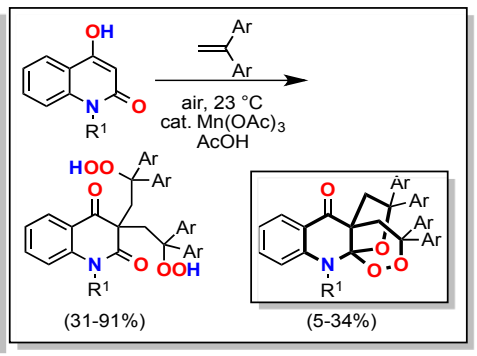

Figure 4