

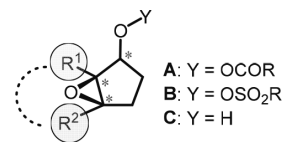
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Development of new innovative synthetic organic reactions using lone pairs of oxygen atoms and their application to natural product synthesis have been studied.

1) Asymmetric synthesis of chiral quaternary Carbon centers: Rearrangement of 1,2-epoxy alcohol

derivatives having electron-withdrawing protective groups such as acyl or sulfonyl group (**A**, **B**) was developed leading to the asymmetric construction of chiral quaternary carbon centers. Domino reaction of 1,2-epoxy alcohols (**C**) and hypervalent iodine reagent afforded the lactols with chiral quaternary center in a single operation.

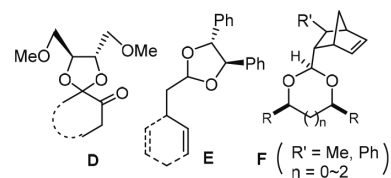


2) Asymmetric synthesis using acetals: Nucleophilic 1,2-addition of Grignard reagents to the α -keto acetals (**D**)

derived from chiral C₂-symmetric diol, 1,4-dimethoxy-2,3-butanediol,

attains the construction of chiral *tert*-alcohols in a highly diastereoselective manner. Intramolecular haloetherification of chiral ene or diene acetals (**E**)

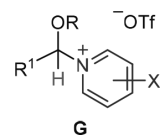
derived from chiral hydrobenzoin affords the compounds with several chiral centers at the remote positions in one-pot operation. In contrast, asymmetric desymmetrizations of *meso*-1,2- to *meso*-1,4-diols is achieved by intramolecular bromoetherification of chiral ene acetals (**F**), derived from optically pure norbornene aldehyde derivatives and *meso*-diols, as a key reaction.



3) Organic chemistry using acetal-type reactive salt chemical species

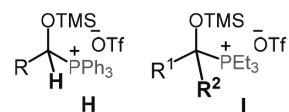
Reactions using pyridinium-type salt chemical species: The combination of TESOTf and pyridine-type base such as 2,4,6-collidine gives the pyridinium-type salt (**G**) from an acetal

of an aldehyde in the presence of a ketal. It makes unprecedented selective hydrolysis of an acetal possible in the presence of a ketal. Acid labile substrates and reagents are available by using pyridinium-type intermediates, since the reaction proceeds under weakly basic condition and the intermediates react with nucleophiles easily. Acetal-type protective groups of hydroxyl functions, such as THP, MOM, MEM, BOM, and SEM groups, are also deprotected in reverse order from the usual methods via the pyridinium-type intermediates.



In situ protection method: Treatment of the mixture of a ketone and an aldehyde with TMSOTf and PPh₃ gives phosphonium salt (**H**) from an aldehyde selectively.

The use of Et₃P in place of PPh₃ gives phosphonium salt (**I**) from a ketone. Using such phosphonium salt as *in situ* protecting group, lower reactive carbonyl functions are transformed and then the phosphonium salts are rebirthed to mother carbonyl groups. Selective transformation of one of two carbonyl groups having similar reactivity is also achieved by utilizing their difference in the formation phosphonium salts.



The developed reactions were proven to be valuable by being applied to efficient synthesis of more than 20 natural products. It is especially noteworthy that the reactions using reactive salt chemical species can change the retrosynthesis because they can make possible the coexistence of two functional groups, which can't coexist in usual reactions.

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