

Tentative Outline

Special Thematic Issue for Current Organic Chemistry

Recent Topics in Organohalogen Reagents and Compounds

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Aims & Scope:

Halogens can be incorporated into many useful organic molecules and fine chemicals utilized in a wide range of scientific fields, such as natural products, biologically active compounds, and organic materials. These halogens, as well as halogenated organic compounds, continue to play an important role as resources that make the lives of humans more prosperous. For example, fluorine is essential in the molecular design of medicines, in order to suitably model their characteristics and effectiveness. Chlorine and bromine are not only found in many natural products showing interesting properties, but also utilized as synthetic intermediates for various transformations in modern industrial production. Iodine atoms in organic compounds can easily take hypervalent forms, which are popularly used for oxidation reactions and cross-couplings as a greener alternative to heavy metal oxidants, as well as transition metal catalysts. Recently, halogen bonding interaction has evolved from a scientific curiosity to general chemical strategy, during the design and manipulation of aggregation processes of organic compounds.

This special issue aims to cover the recent synthetic interest in halogen chemistry and unique characteristics of halogen compounds. We welcome review articles dealing with the recent advances on the theme, for example, the synthesis and reaction of unique organohalogen compounds, halogen bond interaction in controlling the synthetic reaction, and halogen atom-controlled unique reactions for the synthesis of organic materials and pharmaceutical compounds.

Keywords: organohalogen compounds, synthesis, reagent, new intermediate, synthetic application, hypervalent iodine compounds, halogen-bonding

Subtopics along with Contributing authors and abstract

The subtopics to be covered within this issue are listed below:

- Organohalogen compounds
- Halogenations
- Halogenating reagents
- Haloniums and related intermediates
- Hypervalent halogens
- Halogen interaction

Title no: 1 Synthetic Advances of Heterocyclic Compounds Using Hypervalent Iodine Reagents

- **Om Prakash**, Emeritus Fellow (UGC), Chemistry Department, Kurukshetra University, dromprakash50@rediffmail.com
- **Abstract:** n/a
- **Keywords:** Hypervalent iodine reagent, heterocycles

Title no: 2 Hypervalent Iodine-Mediated Consecutive Reactions of Alkynes for the Synthesis of Heterocycles

- **Akio Saito and Victor V. Zhdankin**, Division of Applied Chemistry, Institute of Engineering, Tokyo University of Agriculture and Technology and Department of Chemistry and Biochemistry, University of Minnesota Duluth, akio-sai@cc.tuat.ac.jp
- **Abstract:** Catalytic consecutive reactions could provide not only short-step syntheses without work-up at each step and isolation of many intermediates but clean and atom economical processes. Therefore, toward straightforward and powerful procedures for the construction of heterocycles, we undertake the research on the catalytic consecutive reactions of alkyne compds., which are versatile mol's. In this review, our recent findings on synthetic methods of heterocyclic compds. by means of hypervalent iodine-mediated consecutive reactions are described. That is, (1) syntheses of highly substituted indoles and pyrroles via iodine(III)-mediated Claisen rearrangement reactions of propargylamines, (2) syntheses of oxazoles and furans concomitantly with incorporation of allyl groups or oxygen functional groups via cyclization-allylation sequences or metal-free oxidative cyclization reactions of propargylamides, and (3) syntheses of dihydroquinolines and iminoquinolinones via hetero-ene metatheses of phenylalkynes and aldehydes.
- **Keywords:** Hypervalent iodine reagent, alkyne, cyclization, metal-free synthesis

Title no: 3 Transition Metal-Catalyzed Hypervalent Iodine Coupling Reactions

- **Jian-Wei Han**, Associate Professor, Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, jianweihan@ecust.edu.cn
- **Abstract:** n/a
- **Keywords:** Hypervalent iodine reagent, transition metal catalyst, coupling

Title no: 4 Asymmetric Synthesis Using Chiral Hypervalent Iodine Reagents

- **Ravi Kumar and Tohmas Wirth**, Department of Chemistry, Dyal Singh College and School of Chemistry, Cardiff University, ravi.dhamija@rediffmail.com
- **Abstract:** n/a
- **Keywords:** Hypervalent iodine reagent, chiral reagents and catalysts, asymmetric synthesis

Title no: 5 Recent Advances in Halogen Bond-Assisted Organic Synthesis

- **Tsutomu Konno**, Faculty of Molecular Chemistry and Engineering, Kyoto Institute of Technology, konno@kit.ac.jp
- **Abstract:** Halogen bond interactions, which take place between an electrophilic halogen and the electron-pair of a Lewis base and exhibit high directionality (approximately 180°), are non-covalent bond interactions similar to the hydrogen bond interaction. Many reports on halogen bond interactions have been published thus far, but many of them discuss halogen bond in the context of crystal engineering or supramolecular architecture. Since a seminal report by Bolm in 2008, halogen bond-assisted or -promoted organic synthesis has received significant attention. This review aims to introduce the molecular design of suitable halogen bond donors and organic transformations involving halogen bond interactions to afford a variety of organic compounds.
- **Keywords:** Halogen-bonding interaction, halogen catalyst, non-classical Lewis acid

Title no: 6 New Halogenating Reagents for the Synthesis of Complex Halogen Compounds

- (awaiting responses from potent contributor)
- **Abstract:** A review on halogenation (bromination and chlorination) and halogenating agents of organic compds. in synthesis of complex halogen-containing compounds. The versatility of these

reagents is further explored by combination with solid supported catalysts. The reagents are mild, compatible with many functional groups, and selective towards specific functional groups, which enable the reactions to be used in a variety of applications. These reagents have proven suitable for micro scale synthesis esp. in the solid phase application.

- **Keywords:** Halogenation, halogenating reagent, stereoselective synthesis, halogenated organic compounds

Title no: 7 Highly Selective Hydroiodination of Carbon–Carbon Double or Triple Bonds

- **Akiya Ogawa**, Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, ogawa@chem.osakafu-u.ac.jp
- **Abstract:** Iodine is an element that exhibits characteristic features of heavy halogen, and several compounds containing iodine constitute important synthetic intermediates due to synthetically easy manipulation. To utilize iodine units for organic synthesis, a highly regioselective and stereoselective introduction of iodine to versatile building blocks is significant, and a lot of researches for the selective introduction of iodine to alkynes or alkenes have been investigated. In this review article, we describe regioselective and stereoselective hydroiodination to multiple bonds of building blocks, and its synthetic applications as key intermediates to construct several important compounds.
- **Keywords:** Iodination, stereoselective synthesis, alkene and alkyne activations

Title no: 8 New Transformations Controlled by Halogen Atom in Organic Molecules

- (awaiting responses from potent contributor)
- **Abstract:** Construction of lactone skeleton is an important process to synthesize useful compounds containing various natural products with interesting bioactivity. Conventional intramolecular cyclization strategy based on the use of condensation reagents for carboxylic acids has been contributed to the synthesis of many lactone compounds. In recent years, C-H lactonization reactions of keto acid without requiring these treatments have attracted significant attention.

Recently, Favorskii-type C-H lactonization of haloketo acid was discovered from multiple decomposition reactions during monochlorodimedone assay for evaluation of the oxidative bromination activity of haloperoxidases. This reaction is a unique selective *exo*-cyclization in aqueous solution of weak inorganic base without the use of any sacrificial reagent and external catalyst. Interestingly, monohaloketo acids and di- and tri-haloketo acids under weakly basic conditions selectively gave different products, oxolactone and haloacyllactones, respectively. Their high regioselectivity was controlled by the number of halogen atoms in haloketo acids. On the other hand, *cis*- and *trans*-productivities in the Favorskii type C-H lactonization depend on the substituent positions. Especially, the lactonization of 3-substituted haloketo acids showed high stereoselectivity for production of *trans*-haloacyllactones. Consequently, this selectivity seems to be derived from the steric hindrance during the transient C-H deprotonation step.

In addition to this recent topic, this review deals with reported new transformations controlled by halogen atom in organic molecules.

- **Keywords:** Halogenated molecules, halogen atom effect

Title no: 9 Stereoselective Synthesis of Multisubstituted α -Fluoro- β -Lactams

- **Masanori Omote**, Faculty of Pharmaceutical Sciences, Setsunan University, omote@pharm.setsunan.ac.jp
- **Abstract:** β -Lactams, structures found in β -lactam antibiotics, are the structurally distorted cyclic compounds being subject to nucleophilic acyl substitution reaction. α -Fluorination of β -lactams is a simple and expedient approach to control the reactivity of β -lactam ring toward nucleophilic

attack, which would hopefully lead to new design of future antibiotics. From the viewpoint of obtaining multisubstituted α -fluoro- β -lactams, α -bromo- α -fluoro- β -lactams were considered as key compounds for structure functionalization, including nucleophilic substitution reaction, aldol-type reaction and metal-catalysed cross-coupling reaction. All the reactions were proceeded smoothly to afford a variety of multisubstituted α -fluoro- β -lactams. During the course of the examination, we successfully obtained chiral α,α -difluoro- β -lactams and α -bromo- α -fluoro- β -lactams which were the suitable precursor for making stereocontrolled multisubstituted α -fluoro- β -lactams.

- **Keywords:** Fluorinated β -Lactam, stereoselective synthesis, fluorine atom effect, pharmaceutical compounds

Title no: 10 Unique Reactivities of Organofluorine Compounds in Organic Synthesis

- (awaiting response from potent contributor)
- **Abstract:** Fluorinated organometallic compounds serve as versatile reagents for the synthesis of organofluorine compds. Most reactions start from Lewis base activation of carbon-metal bond through the intermediacy of ate complexes. Interaction of these species with suitable electrophiles leads to products of nucleophilic fluoroalkylation; an alternative pathway involves generation of difluorocarbene. These reagents can also be considered as equiv. of difluoromethylene radical anion and bis(carbanion) when carbon-heteroatom bond C-X is activated. The examples are described in this review.
- **Keywords:** Organofluorine compounds, fluorine atom effect, new building block

Schedule:

- ✧ Manuscript submission deadline: Jan 2020
- ✧ Peer Review Due: Feb 2020
- ✧ Revision Due: Mar 2020
- ✧ Announcement of acceptance by the Guest Editors: Apr 2020
- ✧ Final manuscripts due: May 2020

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