HL
http://heteroletters.org

ISSN: 2231 – 3087(print)
ISSN: 2230 – 9632 (Online)
Coden HLEEAI
Vol. 4: (3), 2014, 467-470

MY LOVE WITH IODINE

Bimal K. Banik*

Department of Chemistry, The University of Texas-Pan American, 1201 West University Drive, Edinburg, TX 77439, USA; bimalbanik10@gmail.com

Key words: Iodine, Catalysis, Synthesis, Organic compounds

Abstract: Iodine is readily available and economical. The use of iodine to catalyze numerous reactions for the preparation of organic compounds has been demonstrated.

Introduction:

The chemistry and biology of molecular iodine and iodine-containing compounds have been investigated extensively. Many iodine containing compounds have medicinal activities and iodine has direct effects on animals and human health. Our research on molecular iodine-catalyzed reaction has proved to be useful for the synthesis of different types of organic compounds. Clearly, the successful realization of many carbocyclic and heterocyclic compounds by catalytic amount of iodine is an important objective. Iodine is relatively non-toxic, crystalline, economical and a mild Lewis acid.

Like many chemistry students, my endeavor on the use of iodine started when I was a master student. Iodine is a volatile solid and it produces a beautiful purple/violet vapor in a closed container. I first used iodine for Thin Layer Chromatography study for the detection of number of compounds and/orto identify the purity of a compound present in an unknown or known synthetic or natural product sample. Then, I started to use iodine to activate the surface of magnesium and zinc metal for Grignard and Reformatsky reaction. Addition of a small pinch of iodine had a profound effect on the metal-mediated reactions. I used to wonder how this small amount of iodine can really activate the metal and therefore, control the complex reaction methods. Gradually, I fell in love with iodine and used this element on several reactions. Of course, the results were so gratifying that we are still using iodine in many of our methods.

Results and Discussions:

During the course of investigation of complex natural product synthesis, we came across a reaction of preparing a highly functionalized alkene from a tertiary alcohol. Due to the acidity of iodine, a cyclization reaction with the aromatic group through a stable tertiary cabocation formation was the expected outcome. Cyclization of the same tertiary alcohol with acid (CH_3SO_3H, HCl, $BF_3.Et_2O$, etc.) produced mainly a *trans*A/B ring system present in many natural terpenoids, alkaloids and steroids as the major products. However, cyclization of the

corresponding alkene produced by the iodine-treatment with acid under identical conditions afforded a mixture of *cis* and *trans*compounds in almost equal quantities.[1]This observation was rationalized through a mechanism. As a result of different course of reactions, synthesis of natural products with*cis* and *trans*-A/B ring junction was possible.

During the course of investigation of beta-lactam chemistry, it was found that a spot of a ketal containing compound in a TLC chamber changes to another high polar compound after a few hours. This observation was eye opening to me. The first impression was that the corresponding beta-lactam is not stable. A reaction of the same beta lactam with small amount of iodine was performed separately and a polar compound was observed. This was isolated and characterized. It was a diol formed through the deprotection of the ketal group. Later, this diol and related diols were used extensively for the preparation of amino sugars, amino acids, alkaloids and polycyclic beta-lactams.[2]

As an extension, severaloxygen-glycosides were cleaved to the parent alcohols by molecular iodine. Since protection and deprotection are reversible process, we became successful in protecting carbonyl groups as acetals, ketals, thioketal and mixed ketals as well as their deprotection with molecular iodine. Oximes and hydrazones were deported to carbonyl compounds using iodine-induced reactions. These reactions were useful to demonstrate intramolecularchemoselectivity.

We developed stereospecific synthesis of glycosides derived from hydroxy beta lactams using molecular iodine as the catalyst. Optically active compounds that are present taxoland thienamycin side chains were made using this method. Several indoles, indenes, pyrroles, quinazoline, imidazolesand other heterocyclic compounds were prepared successfully via iodine-catalyzed reactions. Notably, it was possible to add pyrrole system to beta lactams and pyrrole system to indolesthrough iodine-catalyzed chemical manipulations[3]. The role of iodine in these chemical transformations was not established. But, it was important to note that the reactions as mentioned above did not proceed in the absence of catalyst. In some instances, iodometric titration was performed to identify whether iodine was really consumed in the reaction. Surprisingly, sodium thiosulfate titration method indicated no iodine was consumed, yet the reaction proceeded completely.

Samarium-induced chemistry in the presence of iodine was useful to study reduction of carbonyl compounds and imines and reductive dimerization of carbonyl compounds and imines. These reactions did not proceed in the absence of iodine[4]. The success of these reactions was not due to the formation of bivalent samarium species.

Conclusion:

We demonstrated iodine-catalyzedreactions for the synthesis of diverse compounds.Most of the iodine-catalyzed reactions as described above produced products with high yields. Isolation of products from the reaction mixture was very convenient. Some reactions proceeded in the absence of any solvent with 1 mol% iodine. Considering the budgetary restrictions, our iodine-catalyzed reactions are the perfect examples to cut down the cost of research maintaining the standard of good publications. In addition, it was also found that iodine-catalyzed reactions can tolerate microwave-irradiation. On this basis, some of the iodine-catalyzed reactions under microwave irradiation were completed within minutes instead of hours/days. A few compounds prepared by iodine-catalyzed reactions demonstrated anticancer and antibacterialactivities.

Acknowledgment:
I am highly grateful to numerous of my mentors and colleagues, Professors U. R. Ghatak, Professor A. K. Bose, Professor M. S. Manhas, and Professor F. F. Becker. Students and scientists who have participated in this research are mentioned in the reference section. I am also grateful to NIH, NCI, Kleberg Foundation, Stevens Institute of Technology, University of Texas M. D. Anderson cancer Center and University of Texas-Pan American for their support to our research.

References:

1. (a) Banik, B. K.; Chakraborti, A. K.; Ghatak, U. R.; An Efficient Synthesis of 2-Substituted 3,3-Dimethylcyclohexane-1-ones. A Simple Synthetic Route to Podocarpa-8,11,13-triene Intermediates, *J. Chem. Res.***1986**, 406-407; (b) Banik,B. K.;Ghosh, S.; Ghatak, U. R.; Influence of Methoxy-and Methyl-Aromatic Substituents on Stereochemistry of the Products in the Acid-Catalyzed Cyclization of 2-(2-Arylethyl)-1,3,3-trimethyl cyclohexanols: Stereocontrolled Total Synthesis of (±)-Nimbidiol and (±)-Nimbiol, *Tetrahedron,***1988**, 44, 6947-6955; (c) Banik, B. K.; Ghatak, U. R.; An Expeditious Total Synthesis of (±)-Sempervirol, (±)-Sugiol and (±)-Xanthopherol Methyl Ether by Acid-Catalyzed Cyclialkylation Route", *Synthetic Communications*, **1989**, 19, 1351-1367; (d) Ghosh, S.; Banik, B. K. and Ghatak, U. R.; Influence of Electron Donating Aromatic Substituents on the Stereochemistry of the Products in Cycloalkylation of 2-(2-Arylethyl)-3,3-dimethyl-1-methylene cyclohexane and Related Substrates. Mechanisms of Aromatic Cycloalkylation, *J.Chem. Soc., Perkin Trans I*, **1991**, 3189-3193.
2. (a) Bose**,** A. K.;Banik, B. K.; Mathur, C.; Wagle, D. R.; Manhas, M. S.; "Polyhydroxy Amino Acid derivatives via β-Lactams Using Enantiospecific Approaches and Microwave Techniques", *Tetrahedron***2000**, 56, 5603-5619; (b) B K. Banik, M. S. Manhas and A. K. Bose, "EnantiopureHydroxy β-Lactams via Glycosylation", *Tetrahedron Lett.*1997, 38, 5077-5080; (c) Banik, B. K.; Zegrocka, O.; Manhas, M. S.; Bose, A. K. "Enantiomerically Pure β-Lactams with the Thienamycin Side Chain via Glycosylation", *Heterocycles* **1997**, 46, 173-176; (d) Banik, B. K.; Manhas, M. S.; Bose, A. K. "Versatile β-Lactam Synthons: Enantiospecific Synthesis of (-)-Polyoxamic acid", *J. Org. Chem.* **1993**, 58, 307-309. (e) Banik, B. K.; Manhas, M. S.; Bose, A. K. "Stereospecific Glycosylation via Ferrier Rearrangement for Optical Resolution", *J. Org. Chem.*1994, 59, 4714-4716; (f) Banik, B. K.; Ed. β-Lactams: Synthesis, Stereochemistry, Synthons and Biological Evaluation*, Curr. Med. Chem*., **2004**, Volume 12; (g) Banik, B. K.; Becker, F. F.; Selective Anticancer Activity of β-Lactams Derived from Polyaromatic Compound, *Mol. Med. Rep*., **2010**, 3, 315-316; (h) Banik, B. K.; Banik, I.; Becker, F. F.; Novel Anticancer β-Lactams, *Topics inHeterocyclic Chemistry*, **2010**, 22, 349-373; (i)Banik, B. K.;Banik, I.; Becker, F. F.; Asymmetric Synthesis of Anticancerβ-Lactams*via* Staudinger Reaction: Utilization of Chiral Ketene from Carbohydrate, *Eur. J. Med. Chem*., **2010**, 45, 846-848; (j)Banik, B. K.;Samajdar, S.; Becker, F. F.; Asymmetric Synthesis of Anticancerβ-Lactams*via* Staudinger Reaction, *Mol. Med. Rep*.; **2010**, 3, 319-322.
(k)Banik, B. K.; Zegrocka, O.; Manhas, M. S.; Bose, A. K.;A Facile Iodine-catalyzed Glycosylation: Enantiomerically Pure β-Lactams with the Thienamycin Side Chain;*Heterocycles*; **2009**, 78, 2443-2454;(l) Banik, B. K.; Negi, M.; Manhas, M. S.; Bose,A. K.;

Chemoenzymatic Preparation of Intermediates for The Taxol Side Chain and Analogs, *Mol. Med. Rep*., **2010**, 3, 317-318; (m) Suffness, M.; *Taxol Science and Applications CRC Press*; **1995**.

3. For iodine-catalyzed reactions, see: (a) Samajdar, S.; Basu, M. K.; Becker, F. F.; Banik, B. K., "A New Molecular Iodine-Catalyzed Thioketalization of Carbonyl Compounds: Selectivity and Scope", *Tetrahedron Lett.,***2001**, 42, 4425-4428; (b) Basu, M. K.; Samajdar, S.; Becker, F. F. ; Banik, B. K.,"A New Molecular Iodine-CatalyzedAcetalization of Carbonyl Compounds", *Synlett*, **2002**, 319-321; (c)Banik, B. K.; Samajdar, S.; Banik, I.; "Simple Synthesis of Substituted Pyrroles", *J. Org. Chem.***2004**, 69, 213-216; (d) Banik, B. K.; Chapa, M.; Marquez, J.; Cardona, M.; "A Remarkable Iodine-Catalyzed Protection of Carbonyl Compounds", *Tetrahedron Lett.,***2005**, 46, 2341-2343;(e) Banik, B. K.; Farnandez, M.; Alvarez, C.; "Iodine-Catalyzed Michael Reaction of Indoles Under SolventlesConditions", *Tetrahedron Lett.,* **2005**, 46, 2479-2482;(f) Banik, B. K.**;** Garza, R.; "Iodine-Catalyzed Facile Deprotection of Acetal and Ketal in Acetone",*Chem. Edu.,***2007**, 12, 75-76;(g)Banik,B. K.; Garcia, I.; Morales, F.; Aguilar, C.; "Novel Synthesis of Substituted Pyrroles Bound to Indolinone via Molecular Iodine-Catalyzed Reaction",*Heterocyclic Communications*, **2007**, 13, 109-112; (h) Banik, B. K.; Mukhopadhya, C.; Logan, C.; "Optical Resolution of Dibenzofluorenol: Intermediates for Anticancer Agents; (i) Banik, I. Samajdar, S,; Basu, M. K.; Banik, B. K. "Molecular Iodine-Catalyzed Protection of Carbonyl Compounds", *Heterocyclic Letters*, **2011**, 111-118;(j) Banik, B. K.**;** Manhas, M. S. "Iodine-Catalyzed Stereospecific Glycosylation of Alcohols: Enantiopure β-Lactams", *Tetrahedron Symposium-in-Print*, **2012**, 68, 10769-10779; (k) Bandyopadhyay, D.; Cruz, J.; Jadav; R. N.; Banik, B. K. "An Expeditious Iodine-Catalyzed Synthesis of 3-Pyrrole Substituted 2-Azetidinones", *Molecules*, **2012**, 17, 11570-11584.

4. For samarium-induced iodine-catalyzed reactions see:(a)Banik, B. K.;Samajdar, S.;Ghatak, A.;"A Convenient Samarium-Mediated Reduction of Ferrocenyl Imines", *Heterocycles***, 2001**, 55, 1957-1961; (b)Banik, B. K."Samarium-Induced Reductive Dimerization of Aryl Ketones in Aqueous Alcohol", *Chemistry-An IndianJournal*, **2003**, 1, 149.; (c) Samajdar, S.; Banik, B. K., "Samarium-Induced Reductive Dimerization of Ketimines", *Chemistry-An Indian Journal*,**2003**, 1, 230; (d) Banik,B. K.;Venkatraman, M. S.; Banik, I.; Basu, M. K. "Samarium-Induced Reductive Dimerization of Methyl Cinnamate: Synthesis of 2,8-Diamino Chrysene", *Tetrahedron Lett.,***2004**, 45, 4737-4739; (e) Banik, B. K.; Banik,I.; Aounallah, N.; Castillo, M.; "Samarium-Induced Convenient Reductive Dimerization of Aromatic Ketones: A Mechanistic Approach", *Tetrahedron Lett.,* **2005**, 46, 7065-7068.

Received on May 25, 2014.