SYNLETT
Spotlight 356

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Isatoic Anhydride

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Sudipta Raha Roy was born in West Bengal, India. After receiving his M.Sc. degree from the Visva-Bharati University in Organic Chemistry, he joined the National Institute of Pharmaceutical Education and Research (NIPER), Mohali, India in 2007. Currently, he is working towards completion of his Ph.D. thesis under the supervision of Professor Asit K. Chakraborti as CSIR senior research fellow. His primary research interests focus on the catalytic application of ionic liquids and the mechanistic aspects for the development of environmentally benign organic transformation.

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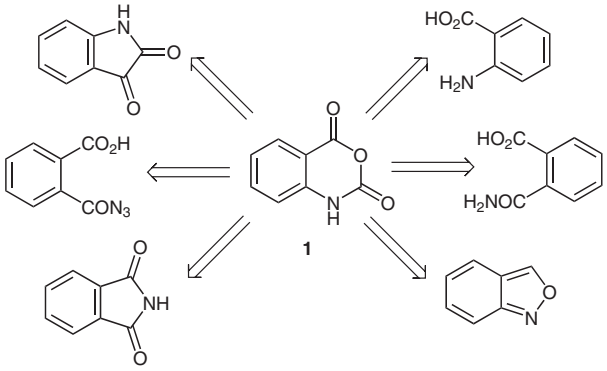
Introduction

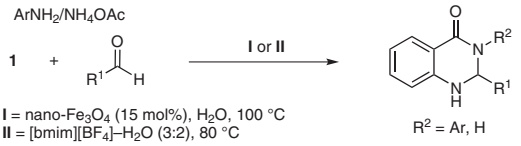
The abundance of heterocyclic motifs in bio-active natural products challenges many researchers to acquire such heterocyclic compounds in the laboratory level. The progress of green chemistry in the synthetic process favors the tandem reactions over the multistep synthesis. Isatoic anhydride (**1**) is a fascinating molecule with a broad spectrum in the synthesis of pharmaceuticals and natural products by tandem reactions. It is commercially available and can be synthesized by different approaches (Scheme 1).[1]



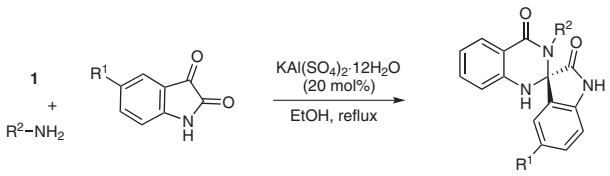
Scheme 1 Synthesis of isatoic anhydride (**1**)

Abstracts

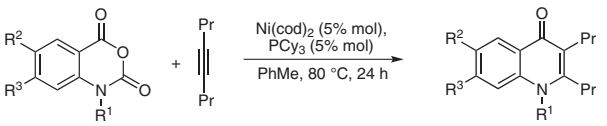
(A) *2,3-Dihydroquinazolin-4(1H)-ones:*
This molecular framework possess a wide range of pharmaceutical activities, for example, they are used as antifertile, antibacterial, and antifungal agents. The compounds can be synthesized by cyclocondensation of **1**, amines, and aldehydes in the presence of Fe_3O_4 nanoparticles or ionic liquid in water.[2]



(B) *1′H-Spiro(isoindoline-1,2′-quinazoline)-3,4′(3′H)-dione:*
Spirooxindole derivatives show very good therapeutic action as anticancer, diuretic, and analgesic agents. These heterocyclic compounds can be synthesized by the tandem reaction of isatin, aldehydes, and amines in the presence of potassium alum.[3]



(C) *Quinazolin-4-ones:*
Isatoic anhydride is an excellent precursor for the decarboxylative carboamination of alkynes to give quinazolin-4-ones. For this chemical transformation $Ni(cod)_2$ is used as efficient catalyst.[4]



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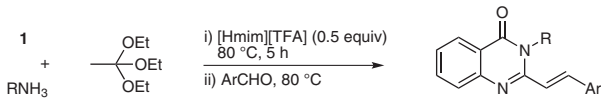
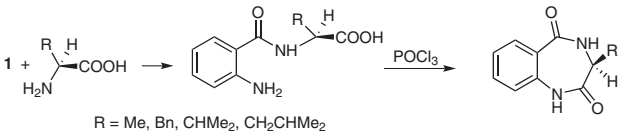
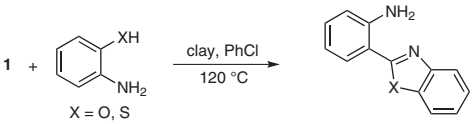
(D) *2-Styrylquinazolin-4-ones:*
2-Styrylquinazolin-4-ones are associated with inhibitory effects on the tubulin polymerization. [Hmim][TFA] serves as a dual-purpose catalyst to construct the 2-methyl-quinazolin-4-ones as well as the Knoevenagel condensation with aldehydes to form the final products.[5]



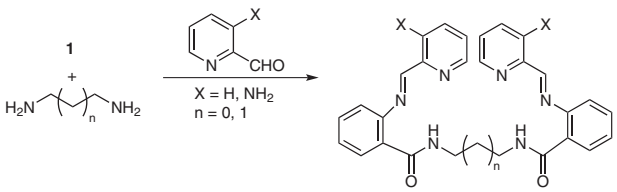
(E) *2,3-Dihydroquinazolin-4(1H)-ones:*
This molecular framework achieved popularity due to its potential application as antithrombotic and antitumor agents. Amino acids react with **1** to form amides, which cyclized under treatment with $POCl_3$ to form the final product.[6]



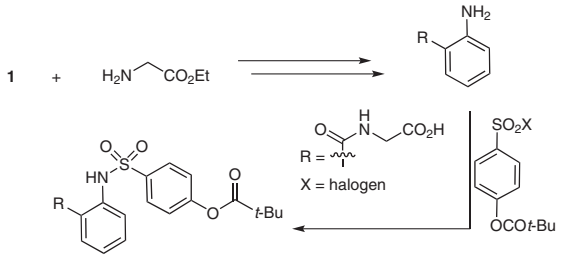
(F) *2-Arylbenzoxazole/benzthiazoles:*
These molecules are widely used in pharmaceutical as well as in non-pharmaceutical industries and can be synthesized by cyclocondensation of **1** with 2-aminothiophenol or 2-aminophenol.[7]



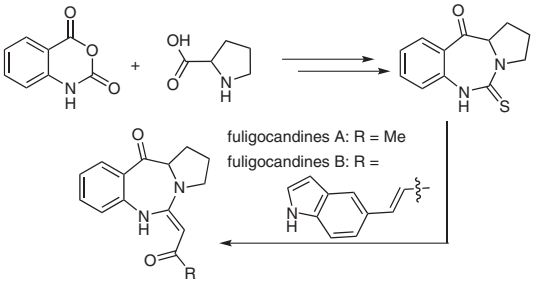
(G) *Polydentate ligands:*
The synthesis of polydentate ligands for the supramolecular chemistry gained a new momentum in the field of bioorganic chemistry. Schiff's bases are very popular to construct the macrocyclic ligands. Diamines and aldehydes are being subsequently used with **1** to construct polydentate ligands.[8]



(H) *Sivelestat sodium*:
This molecule is used for the treatment of acute lung injury associated with the systematic inflammatory response syndrome. It is also used in the composition of antiwrinkle cosmetics. The treatment of **1** with glycine ethyl ester first forms an amide, which subsequently reacts with pivaloyloxy benzene sufonyl chloride to form Sivelestat.[9]



(I) *Fuligocandines A and B*:
These two natural products were isolated from myxomycete *Fuligo candida*. They are biologically potent to sensitize leukemia cells to apoptosis caused by the tumor necrosis factor related apoptosis-inducing ligand. An Eschenmoser episulfide contraction is the key step to synthesize the bioactive cycloanthranilylproline derivative.[10]



References

(1) Deligeorgiev, T.; Vasilev, A.; Vaquero, J. J.; Alvarez-Builla, J. *Ultrason. Sonochem.* **2007**, *14*, 497.
(2) (a) Zhang, Z. H.; Lu, H. Y.; Yang, S. H.; Gao, J. W. *J. Comb. Chem.* **2010**, *12*, 643. (b) Chen, J. X.; Su, W. K.; Wu, H. Y.; Liu, M. C.; Jin, C. *Green Chem.* **2007**, *9*, 972.
(3) Mohammadi, A. A.; Dabiri, M.; Qaraat, H. *Tetrahedron* **2009**, *65*, 3804.
(4) Yoshino, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2009**, *131*, 7494.
(5) Dabiri, M.; Baghbanzadeh, M.; Delbari, A. S. *J. Comb. Chem.* **2008**, *10*, 700.
(6) Bakavoli, M.; Davoodnia, A.; Shahnaee, R. *Chin. Chem. Lett.* **2008**, *19*, 12.
(7) Gajare, A. S.; Shaikh, N. S.; Jnaneshwara, G. K.; Deshpande, V. H.; Ravindranathan, T.; Bedekar, A. V. *J. Chem. Soc., Perkin Trans. 1* **2000**, 999.
(8) Swamy, S. J.; Suresh, K.; Someshwar, P.; Nagaraju, D. *Synth. Commun.* **2004**, *34*, 1847.
(9) Bijukumar, G.; Maloyesh, B.; Sampat, S. S.; Bhirud, S. B.; Rajendra, A. *Synth. Commun.* **2008**, *38*, 1718.
(10) Pettersson, B.; Hasimbegovic, V.; Bergman, J. *Tetrahedron Lett.* **2010**, *51*, 238.