SYNLETT
Spotlight 346

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

Iron–Acetic Acid: A Versatile Reductive Cyclizing Agent

Compiled by Chintakunta Ramesh

Chintakunta Ramesh was born in Kannapoor, Adilabad (Dist), Andhrapradesh, India in 1982. He received his B.Sc. (2002) and M.Sc. in Organic Chemistry (2004) from the Osmania University, Hyderabad, India. Then, he joined EXPICOR Pharma Pvt. Ltd, Hyderabad, as Research Chemist, and later NYCOMED Pharma Pvt. Ltd (ALTANA Pharma Pvt. Ltd), Mumbai, as Junior Research Associate. He is currently pursuing his Ph.D. degree under the supervision of Prof. Ching-Fa Yao at the National Taiwan Normal University, Taiwan, ROC. His current research interests are the development of novel synthetic methodologies and the synthesis of nitrogen- and oxygen-containing bioactive heterocyclic molecules via reductive cyclization of aromatic nitro compounds.

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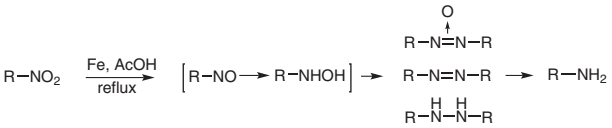
Dedicated to my Ph.D supervisor Prof. Ching-Fa Yao for his constant support and encouragement

Introduction

The iron–acetic acid system is an efficient agent for the reduction of aromatic nitro compounds into its corresponding amines. This transformation proceeds via the hydroxylamine, followed by azoxy and azo compounds to its corresponding aryl amines (Scheme 1).[1] This system was discovered by Bechamp over 100 years ago.[2] However, the first published systematic study of the reduction of nitro compounds by iron–acetic acid appeared in 1977.[3]

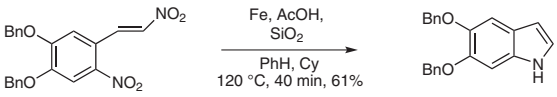
In recent years, iron–acetic acid is widely used for the reduction of nitro groups and subsequent cyclization in a variety of chemical transformations to synthesize biologically important structural units present in heterocyclic molecules. Iron powder is commercial available, of low cost, non-toxic, and environmentally friendly. In addition to this, its functional group tolerance, avoiding of side products, short reaction times, and a simple workup procedure makes iron–acetic acid a versatile reagent.



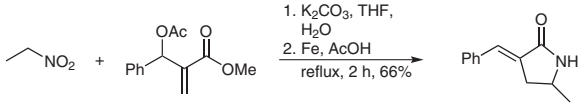
Scheme 1

Abstracts

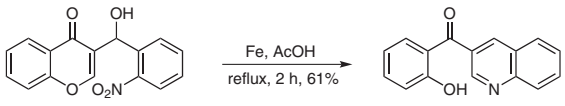
(A) Baldwin and co-workers have reported the reductive cyclization of substituted dinitrostyrene to indole derivatives with iron powder in acetic acid. They noticed some improvement in yield over the standard conditions.[4]



(B) A convenient, operationally simple, one-pot synthesis of various substituted γ-lactams using an S_N2' reaction of acetates of Baylis–Hillman adducts with nitroalkanes followed by reductive cyclization with iron–acetic acid was reported by Basavaiah and co-workers.[5]



(C) Basavaiah et al. have reported an easy, convenient, and operationally simple one-pot procedure for the synthesis of 3-benzoylquinoline derivatives from Baylis–Hillman alcohols using iron–acetic acid.[6]



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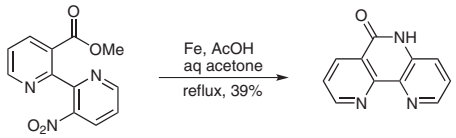
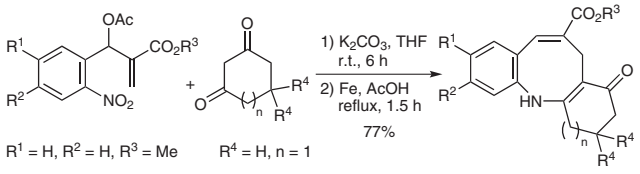
(D) Warnmark and co-workers have presented the synthesis of 2-pyridone fused 2,2′-bipyridine derivatives by reductive cyclization of 2,2′-bipyridine derivatives using iron–acetic acid. Initially, 2,2′-bipyridine derivative were derived via Ullman coupling.[7]

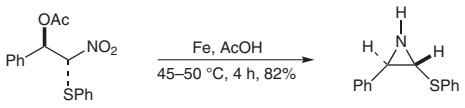


(E) The Baylis–Hillman acetates have been conveniently transformed into tri- or tetracyclic heterocyclic frameworks containing an important azocine moiety via a one-pot multistep protocol involving alkylation followed by subsequent reductive cyclization using iron–acetic acid.[8]

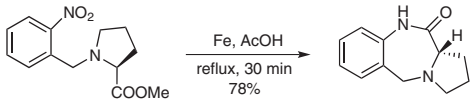


R^1 = H, R^2 = H, R^3 = Me R^4 = H, n = 1

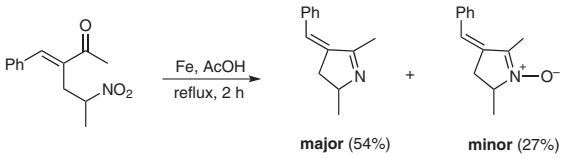
(F) Yadav and co-workers have reported the synthesis of aziridine derivatives by reductive cyclization of 1,2-acetoxysulfenyl nitroalkanes using iron–acetic acid.[9]



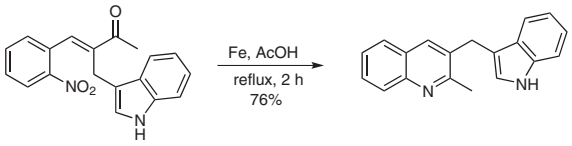
(G) Panda and Mishra have described an efficient method to synthesize a diverse range of [1,4]benzodiazepine skeletons in only two synthetic steps: coupling of 2-nitrobenzyl bromide with a diverse range of chiral amino acids and reductive cyclization with iron–acetic acid.[10]



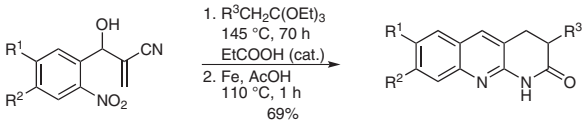
(H) Kim and co-workers disclosed the synthesis of the cyclic nitrone and pyrroline derivatives by the use of iron–acetic acid to give the pyrroline derivative as the major product.[11]



(J) Recently, C.-F. Yao and co-workers reported the synthesis of novel indolylquinoline derivatives via reductive cyclization of (*E*)-3-[(1*H*-indol-3-yl)methyl]-4-(2-nitrophenyl)but-3-en-2-one derivatives in the presence of iron–acetic acid.[12]



(K) More recently, Basavaiah et al. have reported a simple, facile and one-pot procedure for the synthesis of tri- and tetracyclic heterocyclic systems containing a [1,8]naphthyridin-2-one framework from the Baylis–Hillman alcohols using iron–acetic acid.[13]



R^1 = H, R^2 = H
R^3 = Me

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