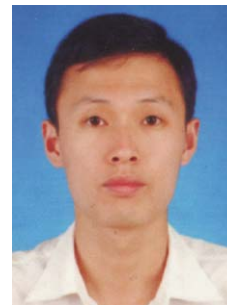


SYNLETT Spotlight 338

Potassium Hexacyanoferrate(II)

Compiled by Jun-Tao Hou



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

Jun-Tao Hou was born in Handan, P. R. of China. He graduated from the College of Handan in 2004 and is currently working towards his M.Sc degree under the supervision of Professor Zhan-Hui Zhang at the Hebei Normal University. His research interest is focused on the development of new synthetic methodologies for green chemistry.

The College of Chemistry & Material Science, Hebei Normal University, Shijiazhuang 050016, P. R. of China
E-mail: juntaohou@gmail.com

Introduction

Potassium hexacyanoferrate(II) has received considerable attention as an environmentally benign cyanide source for the synthesis of a variety of important aryl nitriles. $K_4[Fe(CN)_6]$ is non-toxic {the LD_{50} of $K_4[Fe(CN)_6]$ is lower than that for NaCl} and even used in food industry for metal precipitation. It has also been used as anti-agglutinating auxiliary for table salt (NaCl). It is soluble in water without decomposition even on addition of hydrochloric acid.¹ In addition to its nontoxicity, cheapness, and easy handling, it allows for improved catalyst productivity and substrate scope.² The lower basicity and nucleophilicity of the hexacyanoferrate(II) anion compared to the free

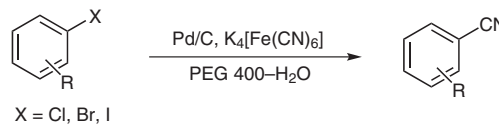
cyanide ion may help to prevent side reactions.³ It has been extensively used as highly efficient cyanation reagent in the synthesis of benzonitriles^{4–17} and (oligo)phenothiazinyl nitriles.¹⁸ It has also reported to be used as the cyanide source for cyanation of aroyl chlorides,¹⁹ heteroaryl halides,²⁰ aryl perfluorooctylsulfonates²¹ and aryl triflates.²² It has been employed in the oxidation of *N*-phenyl-2,5-diarylamino-1,4-benzoquinone imines to 2-(*p*-tolylamino)-5-(*p*-tolyl)phenazin-3-one.²³

$K_4[Fe(CN)_6]$ is commercially available on a ton scale. It can be readily prepared by the reaction of hydrogen ferrocyanide and potassium hydroxide.

Abstracts

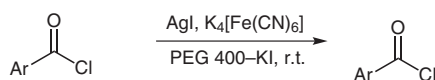
(A) Cyanation of Aryl Halides:

An efficient Pd/C–PEG– H_2O system for the cyanation of aryl halides has been developed by Wan and co-workers.⁷ A wide range of aryl bromides, iodides, and some activated chlorides were cyanated smoothly by using $K_4[Fe(CN)_6]$ as cyanide source.



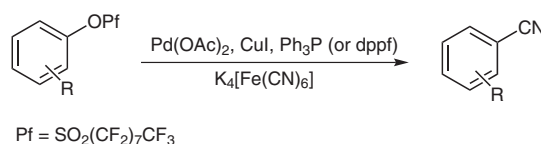
(B) Cyanation of Aroyl Chlorides:

The cyanation of aroyl chlorides by using $K_4[Fe(CN)_6]$ instead of strongly toxic metal cyanides provides a convenient method to prepare aroyl cyanides.¹⁹ The reactions could be efficiently catalyzed by the AgI–PEG 400–KI system under mild conditions.



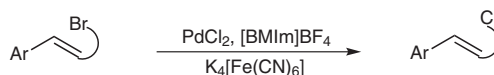
(C) Cyanation of Aryl Perfluorooctylsulfonates:

Zhu and co-workers have reported that aryl perfluorooctylsulfonates can be converted into benzonitriles in the presence of $Pd(OAc)_2$, CuI, and Ph_3P or 1,1-bis(diphenylphosphino)ferrocene (dppf) applying $K_4[Fe(CN)_6]$.²¹



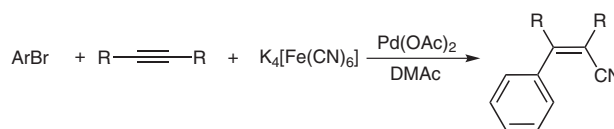
(D) Synthesis of Arylvinyl Nitriles:

The preparation of various arylvinyl nitriles has been achieved by cyanation of the corresponding arylvinyl bromides using $K_4[Fe(CN)_6]$ in ionic liquid under microwave irradiation catalyzed by palladium.²⁴

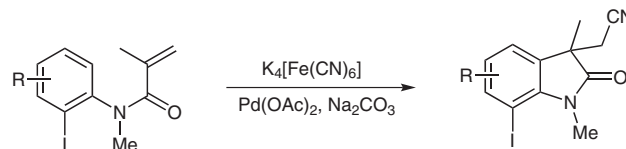


(E) *The Stereoselective Synthesis of Fully Substituted α,β -Unsaturated Nitriles:*

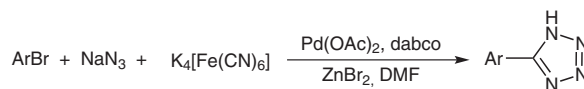
A convenient and practical method for one-pot stereoselective synthesis of fully substituted α,β -unsaturated nitriles from aryl bromides, internal alkynes and $K_4[Fe(CN)_6]$ catalyzed by palladium in *N,N*-dimethylacetamide (DMAc) has been developed.²⁵

(F) *Synthesis of Functionalized 3-Alkyl-3-cyanomethyl-2-oxindoles:*

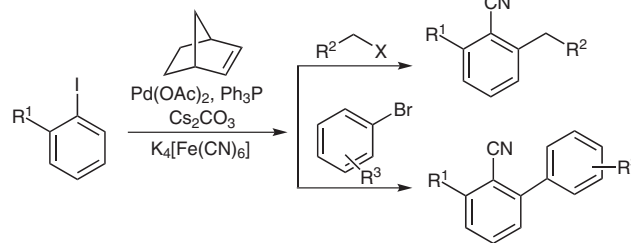
Zhu and colleagues reported an efficient synthetic method for various functionalized 3-alkyl-3-cyanomethyl-2-oxindoles by a domino intramolecular Heck–cyanation sequence using $K_4[Fe(CN)_6]$ as a cyanide donor in the presence of palladium acetate and sodium carbonate.²⁶ The enantiomerically enriched 2-oxindoles were also obtained by this method using (*S*)-Difluorophos as a chiral supporting ligand.

(G) *One-Pot Synthesis of 5-Substituted 1H-Tetrazoles:*

Cai and co-workers reported a new and general method for the one-pot synthesis of 5-substituted 1H-tetrazole through three-component reaction of aryl bromide, NaN_3 , and $K_4[Fe(CN)_6]$ in the presence of catalyst $Pd(OAc)_2$, the additive $ZnBr_2$ and 1,4-diazabicyclo[2.2.2]octane (dabco).²⁷

(H) *Synthesis of Polysubstituted Aromatic Nitriles:*

Lautens and co-workers also showed that a tandem intermolecular *ortho*-arylation–cyanation reaction can be achieved by combining an aryl iodide with an alkyl halide or an aryl bromide followed by cyanation. In this way, polysubstituted aromatic nitriles can be prepared in one step.²⁸



References

- (1) (a) Schareina, T.; Zapf, A.; Beller, M. *J. Organomet. Chem. Commun.* **2004**, 689, 4576. (b) Schareina, T.; Zapf, A.; Beller, M. *Chem. Commun.* **2004**, 1388.
- (2) Schareina, T.; Jackstell, R.; Schulz, T.; Zapf, A.; Cotté, A.; Gotta, M.; Beller, M. *Adv. Synth. Catal.* **2009**, 351, 643.
- (3) Schareina, T.; Zapf, A.; Cotté, A.; Müller, N.; Beller, M. *Synthesis* **2008**, 3351.
- (4) Ren, Y.; Liu, Z.; Zhao, S.; Tian, X.; Wang, J.; Yin, W.; He, S. *Catal. Commun.* **2009**, 768.
- (5) Schareina, T.; Zapf, A.; Mägerlein, W.; Müller, N.; Beller, M. *Chem. Eur. J.* **2007**, 13, 6249.
- (6) Zhu, Y.-Z.; Cai, C. *Eur. J. Org. Chem.* **2007**, 2401.
- (7) Chen, G.; Weng, J.; Zheng, Z.; Zhu, X.; Cai, Y.; Cai, J.; Wan, Y. *Eur. J. Org. Chem.* **2008**, 3524.
- (8) Zhu, Y.-Z.; Cai, C. *J. Chem. Res.* **2007**, 484.
- (9) Weissman, S. A.; Zewge, D.; Chen, C. *J. Org. Chem.* **2005**, 70, 1508.
- (10) Cheng, Y.-N.; Duan, Z.; Li, T.; Wu, Y. *J. Lett. Org. Chem.* **2007**, 4, 352.
- (11) Grossman, O.; Gelman, D. *Org. Lett.* **2006**, 8, 1189.
- (12) Schareina, T.; Zapf, A.; Mägerlein, W.; Müller, N.; Beller, M. *Tetrahedron Lett.* **2007**, 48, 1087.
- (13) Cheng, Y.-N.; Duan, Z.; Li, T.; Wu, Y. *J. Synlett* **2007**, 543.
- (14) Polshettiwar, V.; Hesemann, P.; Moreau, J. J. E. *Tetrahedron* **2007**, 63, 6784.
- (15) Nandurkar, N. S.; Bhanage, B. M. *Tetrahedron* **2008**, 64, 3655.
- (16) Schareina, T.; Zapf, A.; Beller, M. *Tetrahedron Lett.* **2005**, 46, 2585.
- (17) Velmathi, S.; Leadbeater, N. E. *Tetrahedron Lett.* **2008**, 49, 4693.
- (18) Franz, A. W.; Popa, L. N.; Müller, T. J. *J. Tetrahedron Lett.* **2008**, 49, 3330.
- (19) Li, Z.; Shi, S.; Yang, J. *Synlett* **2006**, 2495.
- (20) Schareina, T.; Zapf, A.; Mägerlein, W.; Müller, N.; Beller, M. *Synlett* **2007**, 555.
- (21) Zhu, Y.-Z.; Cai, C. *Aust. J. Chem.* **2008**, 61, 581.
- (22) Zhu, Y.-Z.; Cai, C. *Synth. Commun.* **2008**, 38, 2753.
- (23) Burmistrov, K. S.; Glukh, A. I.; Toropin, N. V. *Russ. J. Org. Chem.* **2005**, 41, 944.
- (24) Li, L.-H.; Pan, Z.-L.; Duan, X.-H.; Liang, Y.-M. *Synlett* **2006**, 2094.
- (25) Cheng, Y.-N.; Duan, Z.; Yu, L.; Li, Z.; Zhu, Y.; Wu, Y. *J. Org. Lett.* **2008**, 10, 901.
- (26) Pinto, A.; Jia, Y.; Neuville, L.; Zhu, J. *Chem. Eur. J.* **2007**, 13, 961.
- (27) Zhu, Y.-Z.; Ren, Y.-M.; Cai, C. *Helv. Chim. Acta* **2009**, 92, 171.
- (28) Mariampillai, B.; Alliot, J.; Li, M.; Lautens, M. *J. Am. Chem. Soc.* **2007**, 129, 15372.