J. Integr. Sci. Technol. 2016, 4(2), 111-120 Article

Journal of Integrated
SCIENCE & TECHNOLOGY

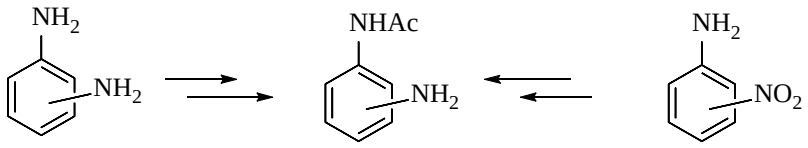
A review on Synthesis of Aminoacetanilides

Raman Singh, Rajneesh Kaur, Kuldeep Singh*

Chemistry Department, M. M. University Mullana – 133207 India

Received on: 29-Apr-2016 Accepted and Published on:17-Sept-2016

ABSTRACT



Aminoacetanilides have many applications in pharmaceutical industry, dyes and pigment industry, and are important intermediates to synthesize various heterocycles and aromatics. This review discusses various synthetic conditions and use of aminoacetanilides.

Keywords: acylation, aminoacetanilides

INTRODUCTION

Aminoacetanilides are the organic compounds having an acetanilide moiety that is –$NHCOCH_3$ group on the benzene ring and an amino group at the perspective positions such as at ortho-, meta- and para- positions and thus are named para-aminoacetanilides, ortho-aminoacetanilides and meta-aminoacetanilides respectively (Figure – 1)**.**

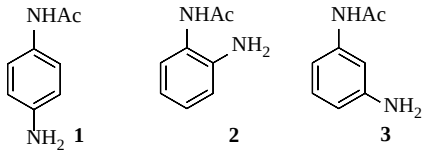


Figure 1: Aminoacetanilides

p-Aminoacetanilide **1** has a leaf or flake like appearance. It is an odourless solid chemical and is usually used as an excellent inhibitor of hydrogen peroxide decomposition. This chemical has found application in the intermediation in dyes and dye intermediate synthesis and camphor synthesis. Besides, this is also used to neutralize cellulose ester vanishes. It is also named as acetamide-*N*-(4-aminophenyl) and IUPAC name is *N*-(4-aminophenyl)acetamide. It belongs to the classes of primary amine, intermediates of dyes and pigments, aromatic carboxylic acids, amides, anilides, anhydrides and salts. It is a kind of white or slightly reddish solid and is slightly soluble in water. It should be stored in airtight, cool and dry place.

o-Aminoacetanilide **2** are also known as 2-(acetamido)aniline. In *o*-aminoacetanilide, amino and acetanilide groups are present at *ortho*- position to each other. Its molecular formula is $C_8H_{10}N_2O$ of molecular weight 150.18g. It is yellow colored solid chemical compound having a melting point in a range of 132-135 ^oC.

m-Aminoacetanilide **3** are also known as 3-(acetamido)aniline. In *m*-aminoacetanilide, amino and acetanilide groups are present at *meta*- position to each other. Its molecular formula is $C_8H_{10}N_2O$ of molecular weight 150.18g. It is a slight green colored solid chemical compound having a melting point in a range of 87-89^oC.

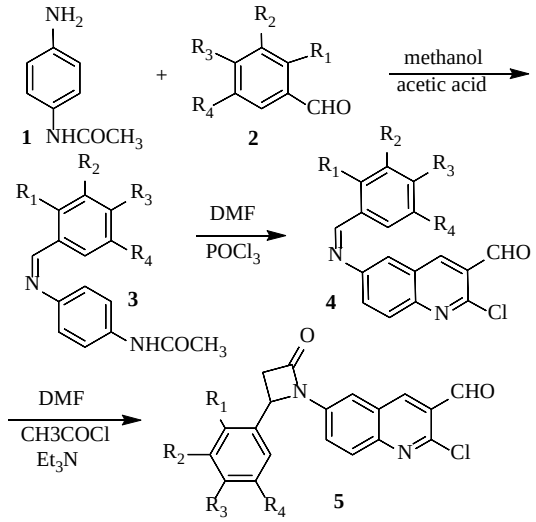
p-Aminoacetanilide is used in the formation of assembly of Au nanoparticles of different sizes. Das & co-workers[4] synthesized citrate stabilized spherical Au nanoparticles and assembled into a linear array, which depends upon the concentration of *p*-aminoacetanilide in the medium. Longer assemblies of Au nanoparticles depends upon the concentration of *p*-aminoacetanilide and high concentration also led to the formation of branched ones. At high concentration, substantial fusion of NPs also occurs.

Corresponding Author: Dr. Kuldeep Singh
Tel: 8059930803
Email: drkuldeepsingh @pundir.in

Cite as: *J. Integr. Sci. Technol., 2016, 4(2), 111-120.*

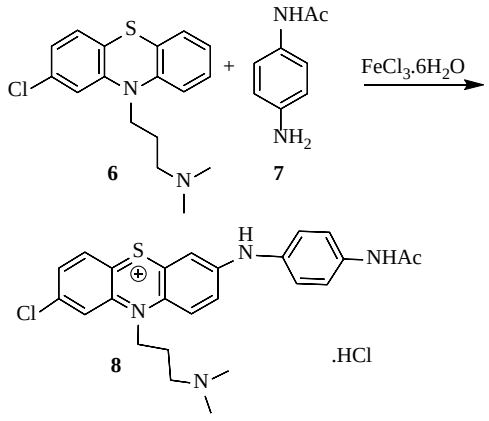
 http://pubs.iscience.in/jist

Gaidhane & co-workers[5] synthesized β–lactam using *p*-aminoacetanilide **1** as starting material. β–lactam have great chemothreaupetic activities and has important application in synthesis of natural and non-natural α-amino acids. They synthesized a series of oxa-azetidin-1-yl-quinoline-3-carbaldehyde by condensation of 4-aminoacetanilide 1 with aromatic aldehyde 2 yielding *N*-(4-(4/-methoxybenzylideneamino)phenyl)acetamide 3, which on reaction with dimethyl formamide in presence of $POCl_3$ formed 6-(4/-methoxybenzylideneamino)-2-chloroquinoline-3-carbaldehyde 4. This Schiff`s based derived quinoline on treatment with acetyl chloride and triethylamine in DMF furnished 2-chloro-6(2/-(4/-methoxyphenyl)-4-oxaazetidin-1-yl)quinolone-3-carbaldehyde 5 (**Scheme 1**).



Scheme 1

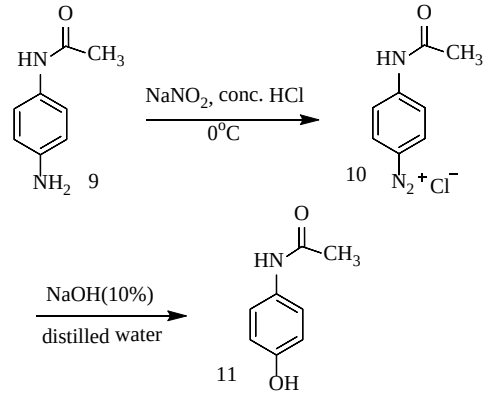
Kaffiji et al.[6] synthesized **8** by interaction of p-aminoacetanilide **7** with 3-(2-chloro-10H-phenothiazin-10-yl)-*N*,*N*-dimethylpropan-1-amine **6** in presence of ferric chloride hexahydrate that is used for the spectrophotometric determination of chloromaprazine HCl in aqueous solution. The method is based on the formation of violet color product **8.** The reaction was studied by UV-VIS spectrophotometric analysis **(Scheme 2).**



Scheme 2

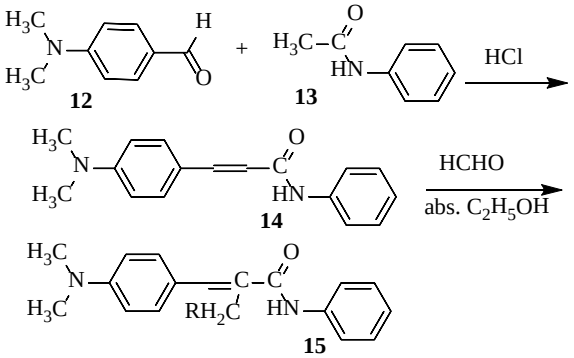
Guma et al[7] synthesized Acetaminophen (*N*-acetyl-*p*-aminophenol) **11** or Paracetamol, IUPAC systematic name 4–Hydroxyacetanilide, $C_8H_9NO_2$, AP) by converting *p*-aminoacetanilide **9** into diazonium salt **10** and then treated with sodium hydroxide solution to get the crude product. *p*-aminoacetanilide **9** was synthesized from acetanilide followed by the nitration and reduction. FTIR spectra and the melting point of the crude product matched with spectra of paracetamol tablets. Paracetamol is one of the most extensively employed drugs in the world, which is used to treat mild to moderate pain as well as for treatment of headache and to reduce pyrexia. It is a valuable non-steroidal anti-inflammatory drug that is widely used for the management of pain and fever, in a variety of patients including children, the elderly and those with osteoarthritis **(Scheme 3)**.

Vilsmeir-Haack[8] reported a simple and regioselective synthesis of 2-chloro, 3-formylquinolines by cyclizationof *N*-arylacetamides. The Vilsmeir-Haack reagent has been proved to be a versatile reagent capable of executing a large variety of synthetic transformations. It finds application in formyaltion, cyclohaloaddition, cyclization and ring annulation. Its potentiality was explored by the synthesis of 4-(*N*,*N*-dimethylaminomethylene)-2-alkyl/aryl-2-oxazolin-5-ones from *N*-acyl derivatives of α-amino acid esters and α-aminoacetanilides. To develop novel quinoline based fused heterocyclic system as potential anti-cancer agents, a quinoline nucleus with different substituents at 2- and 3- positions was required which afforded a versatile synthon for further heteroannulations.



Scheme 3

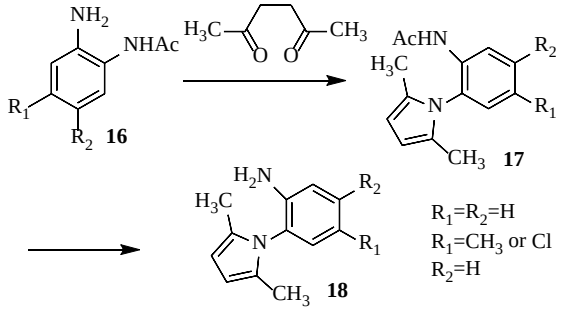
Kalirajan[9] reported synthesis of mannich bases having biological activities. Among the different biological activities, some mannich bases are reported to possess potent local anesthetic activity. For e.g mannich bases of *p*-substituted acetophenones have been reported for potent local anesthetic action.



Scheme 4

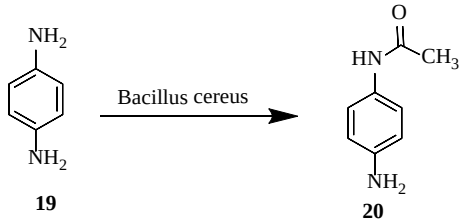
Mannich bases **15** were synthesized from 4-*N*,*N*-dimethylaminobenzylidene acetanilide **14** and reported the local anaesthetic activity and partition coefficient of the synthesized compounds. *p*-dimethylaminobenzaldehyde **12** was treated with acetanilide in the presence of dilute hydrochloric acid to form 4-*N*,*N*-dimethylaminobenzylidene acetanilide.**14** The above compound was treated with secondary amines in ethanol and formaldehyde in acid medium to get converted into Mannich bases **15 (Scheme 4)**.

Hazelwood et al.[10]. synthesized *N*-(*o*-aminoaryl)pyrroles **18** by hydrolyzing *N*-(*o*-acetaminoaryl)pyrroles **17.** The latter was synthesized by treatment of *o*-aminoacetanilide **16** with acetonyl acetone **(Scheme 5)**.



Scheme 5

Verma et al.[11] synthesized a benzothiazole nucleus *N*-(2-aminobenzo[d]thiazol-2-yl)acetamide from *p*-aminoacetanilide, and on treatment with phthalic anhydride produced 2-(6-thiazol-2-yl-carbamoyl)benzoic acid. The synthesized compounds were confirmed by spectroscopic methods. Some of the compounds exhibited potent anti-inflammatory and analgesic activities.

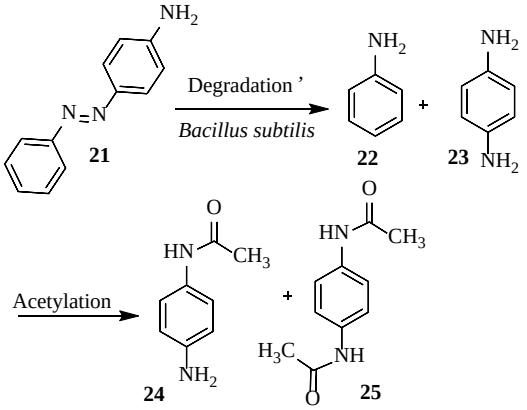


Scheme 6

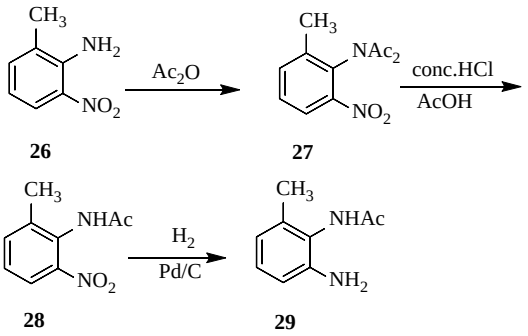
Mulyono et al.[12] isolated a bacterium, *Bacillus cereus* from soil and grown it on medium containing 4-phenylenediamine and polypepton. This Becillus cereus converted a wide variety of anilines including 4-phenylenediamine to their corresponding acetanilides. This growing cell acetylated an amino group of 4-phenylenediamine **19** into 4-aminoacetanilide.**20 (Scheme 6)**.

Idaka and co-workers[13] summarized the degradation of *p*-aminoazobenzene **21** by *Bacillus subtilis* producing aniline **22** and *p*-phenylenediamine **23** by reductive fission of an azo bond. The aniline produced on acylation yield *p*-aminoacetanilide **24** and *p*-phenylenediacetanilide.**25 (Scheme 7)**.

Tanaka and co-workers[14] carried out acetylation of 5-methyl-2-nitroaniline **26** to prepare *N*,*N*-diacetyl compound **27** which on partial hydrolysis (using concentrated HCl in acetic acid) produces 5-methyl-2-nitroacetanilide **28**. Catalytic hydrogenation of later gave 2-amino-6-methylacetanilide.**29 (Scheme 8)**.

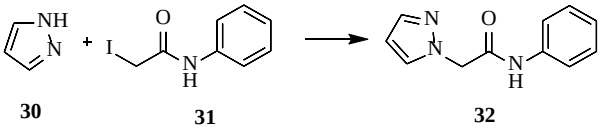


Scheme 7



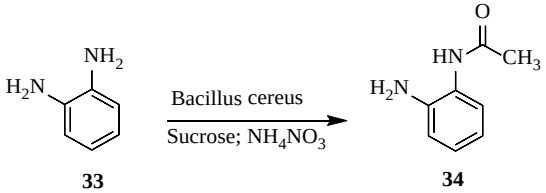
Scheme 8

Lovu et al.[15] carried out synthesis of substituted 2-(pyrazol-1-yl)acetanilide **32** from *N*-alkylation of pyrazole **30** and its derivatives with 2-iodo-*N*-phenylethanamide **31**. These compounds exhibit local anesthetic and antiarrhythmic actions **(Scheme 9)**.



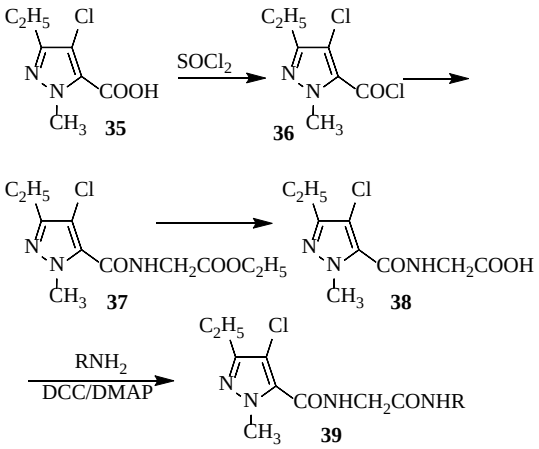
Scheme 9

Takenaka & co-workers[16] studied that Bacillus cereus which was grew on basal medium further supplemented with 2-phenylenediamine **33**, sucrose and ammonium nitrate transform 2-phenylenediamine **33** to 2-aminoacetanilide **34 (Scheme 10)**.



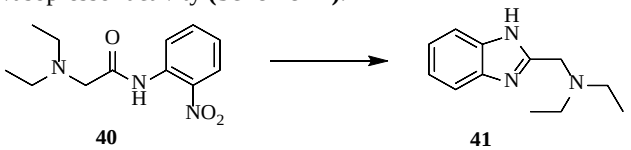
Scheme 10

Fang and co-workers[17] synthesized pyrazole carboxamides **39** containing α-aminoacetanilide moiety which show fungicidal activities against *Rhizoctonia solani*, *Sclerotinia scleotiorum*, *Monilinia fructicola* and *Aleternaria bassicae*. Pyrazole carboxamides containing α-aminoacetanilide was synthesized by condensation of *N*-(4-chloro-3-ethyl-1-methyl-5-pyrazole carbonyl)glycine with substituted aniline or benzyl amine) **(Scheme 11)**.



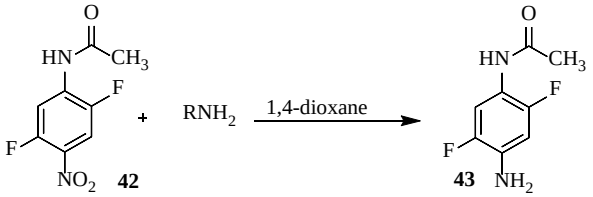
Scheme 11

Erdtmen and Lofgreen in 1937 synthesized α-diethylaminoacetanilide **40**. Which was later used to prepared α-diethylamino-*o*-aminoacetanilide **40** as an intermediate in synthesis of 2`-diethyl aminomethylbenzimidazole **41** which have vasopressor activity **(Scheme 12)**. [18]



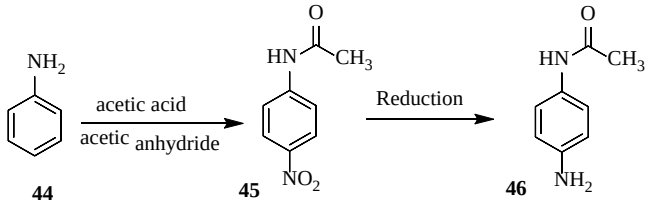
Scheme 12

Haga et al.[19] has synthesized *N*-(4-amino-2,5-difluorophenyl)acetamide **43** from 2,5-difluoro-4-nitroacetanilide **42** with excess of amines in an inert solvent such as 1,4-dioxane, THF, ethylene glycol, dimethyl ether **(Scheme 13)**



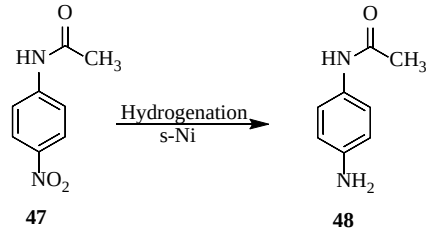
Scheme 13

Yanki[20] has reported synthesis of *p*-aminoacetanilides **46** by the acetylization of aniline **44** with acetic acid and acetic anhydride, producing nitroacetanilide **45** followed by reduction processes (**Scheme 14)**



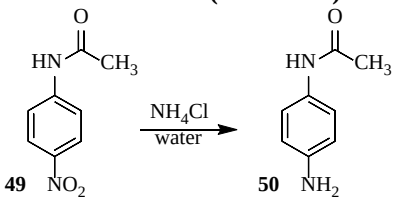
Scheme 14

.Liyu-han et al.[21] reported the synthesis of *p*-aminoacetanilide **48** from *p*-nitroacetanilide **47** by hydrogenation using modified skeletal nickel (s-Ni) as catalyst. The modified s-Ni catalyst was prepared through activation treatment of rapidly quenched Ni-M-Al alloy precursor in NaOH solution **(Scheme 15)**.



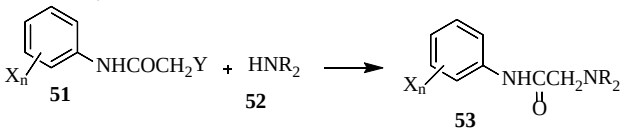
Scheme 15

Zupei et al.[22] carried out a green study on the synthesis of 4-aminoacetanilide **50** by *p*-nitro-aniline **49** using water as solvent and ammonia chloride as reducter **(Scheme 16)**.



Scheme 16

George[23] carried out the synthesis of di-alkenylaminoacetanilides **53** by the reaction of nuclearly halogenated 2-chloroacetanilide **51** with a dialkenylamine **52** **(Scheme 17**).

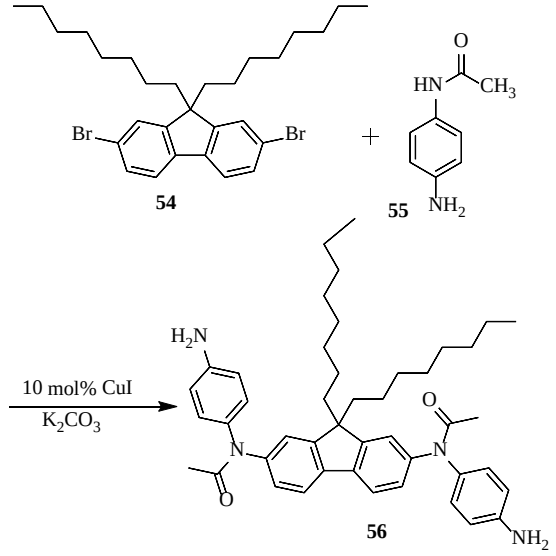


Here X= halogen
n = integer from 1 to 5
R = alkenyl hydrocarbon having 3 to 6 carbon atom
y = halogen

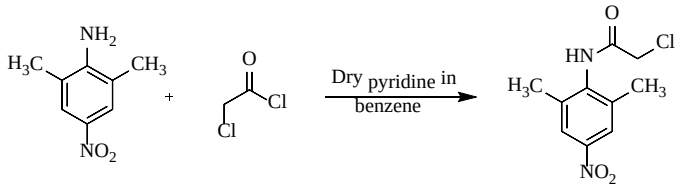
Scheme 17

Shang et al.[24] carried out synthesis of *p*-aminoacetanilide by acetylation. Optimum condition required for reaction of *p*-aminoacetanilide with 2-methyl-5-acetylaminobenzene sulphonyl chloride. Barghamadi & co-workers[25] reported synthesis of a new flourene containing diamine, *N*-[7-(acetyl-4-aminoanilino)-9,9-dioctylflourene-2-yl]-*N*-4-aminophenylacetamide **56** through the reaction of 2,7-dibromo-9,9-di-octylflourene **54** with 4-aminoacetanilide **55** in the presence of 10 mol% CuI, 20mol%, *N*,*N*`-dimethylethylenediamine as a catalyst and potassium carbonate(K_2CO_3) as a base. They proposed a series of novel polyamides by the direct polycondensation of new diamine with various commercially available aliphatic and aromatic carboxylic acids **(Scheme 18).**

Willman et al.[26] reported synthesis of α-diethylamino-4-amino-2,6-dimethylacetanilide **59** to study their anesthetic activities. Reaction of 2-chloroacetyl chloride **58** with a solution of 4-nitro-2,6-dimethylaniline **57**, dry pyridine in benzene gave α-chloro-4-nitro-2,6-dimethylacetanilide. The product was refluxed with diethylamine to obtain α-diethylamino-4-amino-2,6-dimethyl acetanilide **(Scheme 19)**.

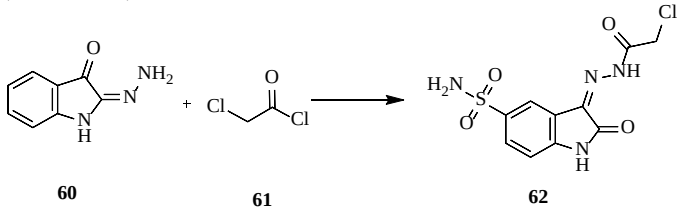


Scheme 18



Scheme 19

Paudala & co-workers[27] synthesized 2-*chloro*-*N*-[(Z)-(2-oxo-5-sulphamoyl-indolin-3-ylidine)amino]acetamide **62** derivatives by refluxing isatin hydrazone **60** with chloroacetyl chloride **61**. These derivatives exhibit antimicrobial and anti-inflammatory activities. The compounds were confirmed by spectrophotometry. These compounds have antibacterial activity against *B.subtilis, B.cereus, S-epidermidis, S.typhi, P.aeruginosa and K.pneumonia* and exhibit antifungal activities against *A.flavus, F.oxysporium, P.notatum (***Scheme 20**).



Scheme 20

Chettur and co-workers[28] synthesized 2-amino(*N*-D-ribosyl)acetamide-5'-phosphate **(Fig. 2)** by condensing 2,3-*o*-isopropylidene-D-ribofuranosylamine-*p*-toluenesulfonate with the mixed anhydride of *N*-(benzyloxycarbonyl)glycine, followed by phosphorylation with 2-cyanoethylphosphate and removal of the protecting groups. By varying the conditions, the α-4 and the β-5 anomers could be obtained and separated from each other.

Fosdick[29] carried out synthesis of α-dialkylaminoacetanilide by the treatment of aniline or nitroaniline in chloroacetyl chloride .using acetone. The obtained oily product was crystallized and after recrystallization with alcohol, yielded α-dialkylaminoacetanilide.

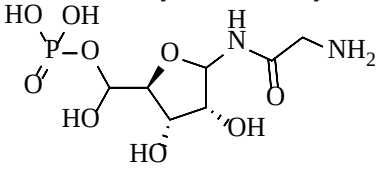
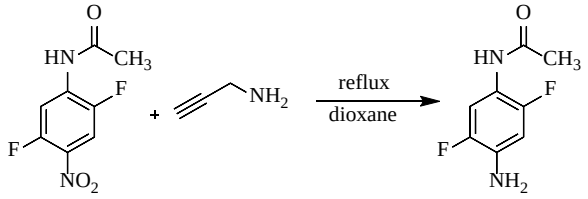


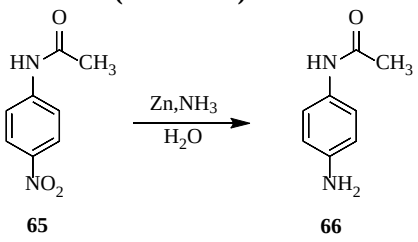
Figure 2

Toru et al.[30] invented method for the production of 2,5-diflouro-4-aminoacetanilide **64** by making use of 2,5-diflouro-4-nitroacetanilide **63** which was dissolved in propargylamine and dioxane followed by heating and refluxing **(Scheme 21)**



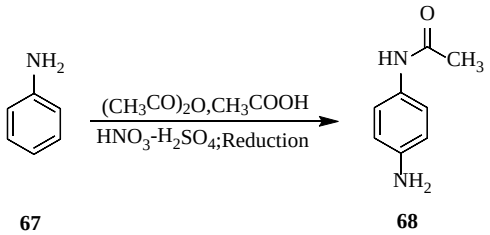
Scheme 21

Cao et al.[31] synthesized *p*-aminoacetanilide **66** by treatment of *p*-nitroacetanilide **65** with water as solvent, followed by reduction with zinc and ammonia **(Scheme 22)**.



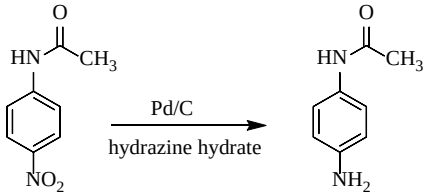
Scheme 22

Yanxi and co-workers[32] carried out synthesis of *p*-aminoacetanilide **68** by acetylization of aniline **67** with acetic acid and acetic anhydride, followed by nitration and reduction **(Scheme 23)**.



Scheme 23

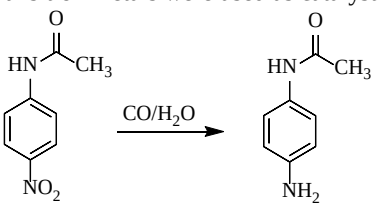
Zhang et al.[33] reported the reduction of *p*-nitroacetanilide **69** by hydrazine hydrate in the presence of Pd/C as catalyst. The amount of the catalyst played a major role in the reduction process. Reaction conditions was the major part for the synthesis of *p*-aminoacetanilide **70 (Scheme 24)**.



69 **70**

Scheme 24

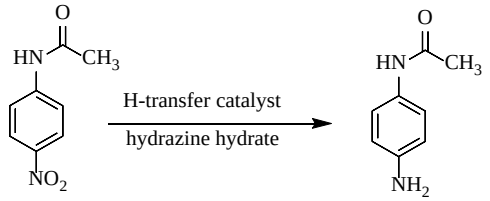
Xiao et al.[34] showed that aromatic amines **72** can be prepared by catalytic reduction of aromatic nitro compounds **71** using CO/H_2O. The carbonyl transition metals were used as catalyst **(Scheme 25).**



71 **72**

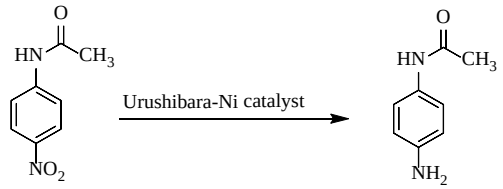
Scheme 25

Wen et al.[35] investigated a new cheap catalyst which was used for the reduction of aromatic nitro compounds **73** with hydrazine hydrate. The catalyst carried out the reduction of substituted nitrobenzene derivatives. They realized that both the properties and position of substituents affect the reduction and the electron attracting group is favourable for the reduction (**Scheme 26)**.



73 **74**

Scheme 26



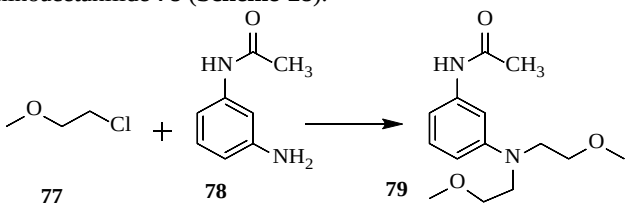
75 **76**

Scheme 27

Jian[36] reported the synthesis of intermediates, 3-(3,4-aminophenyl)-alanine and 3-(*p*-aminophenyl)alanine of new anti-tumour drug, 5% of Pd/Al_2O_3 was used which act as an excellent catalyst. This catalyst is excellent both in activity and selectivity for the hydrogenation of carbon-carbon double bond and the reduction of nitro group. The reaction condition used for hydrogenation and reduction were 50 ± 5^0C at atmospheric pressure. The main advantage of this catalyst is that, these can be recovered and reused**.**

Li et al.[37] carried out the reduction of nitro compounds **75** by Urushibara Nickel catalyst. Urushibara Nickel catalyst can be prepared by reducing nickel chloride with zinc powder (**Scheme – 27**).

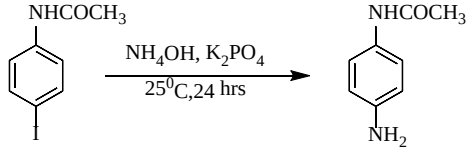
Raman & co-workers[38] synthesized a tridentate Schiff base ligand by the condensation of salicylaldehyde and *p*-aminoacetanilide. These complexes have nuclear activity and cleave DNA through redox chemistry. Study showed that in the presence of H_2O_2, all the complexes are capable of cleaving Lambda DNA. Xiang et al.[39] created some synthetic techniques for the synthesis of 3-(*N*,*N*-dimethoxyethyl)aminoacetanilide **79** optimized from 2-chloro-ethylmethylether **77** and 3-aminoacetanilide **78** (**Scheme-28**).



77 **78** **79**

Scheme 28

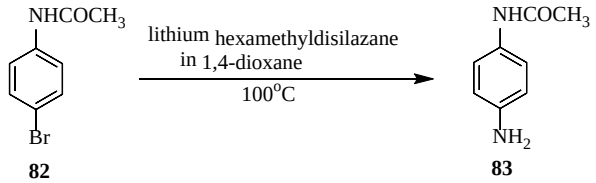
Kumar and Sargal[40] reported fungicidal activities of Co(II), Ni(II) and Cu(II) complexes with Schiff`s bases 3,5-dinitrobenzylidine-2,4-dinitroaniline, 3,5-dinitrobenzylidine-4-aminoacetanilide, 3-nitrobenzylidine-2-aminoacetanilide.



80 **81**

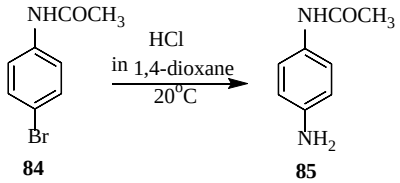
Scheme 29

Wang and coworkers[41] synthesized *p*-aminoacetanilide **81** from *p*-iodoacetanilide **80** by use of ammonium hydroxide, potassium phosphate, 1-(5,6,7,8-tetrahydroquinoline-8-yl)-2-methylpropane-1-one, copper(1)bromide in dimethyl sulphoxide when reaction was carried out at room temperature for 24 hrs in an inert atmosphere in sealed tube **(Scheme 29)**.



82 **83**

Scheme 30

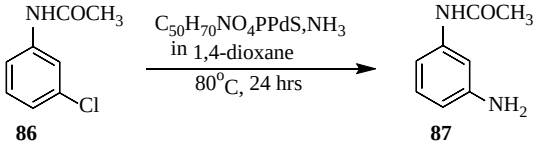


84 **85**

Scheme 31

Harris et al.[42] synthesized *p*-aminoacetanilide **83** from *p*-bromoacetanilide **82** with lithium hexamethyldisilazane, *N*-[2-(dicyclohexylphosphino)-1,1`-biphenyl-2-yl]-*N*,*N*-dimethylamine,

Tris-(dibenzylieneacetone)dipalladiium(0) in 1 4-dioxane at a temperature of 100^{0}C for 17 hrs **(Scheme 30)**.



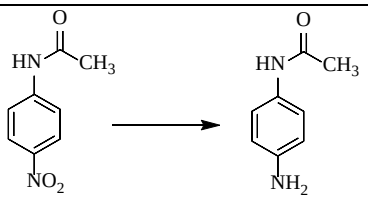
86 **87**

Scheme 32

The same product can be synthesized from the reactant but at different reaction conditions by using hydrogen chloride in 1,4-dioxane at a temperature condition of 20^{o}C for 0.083 hours **(Scheme 31)**.

Cheung et al.[44] reported the synthesis of *m*-aminoacetanilide **87** from *m*-chloroacetanilde **86** on treatment with dicyclohexyl(2`,4`,6`-triisopropyl-5-methoxy-3,4,6-triethyl-[1,1`-biphenyl]-2-yl]phosphine, $C_{50}H_{70}NO_4$ PPdS, dicyclohexyl(2`,4`,6`-triisopropyl-4-methoxy-3,5,6-trimethyl-[1,1`-biphenyl]-2-yl)phosphine, ammonia, sodium-2-butanolate in 1,4-dioxane at a temperature of 80^{0}C for 24 hours in an inert atmosphere. The yield of *m*-aminoacetanilide **87** obtained from *m*-chloroacetanilde **86** was 48% **(Scheme 32)**.

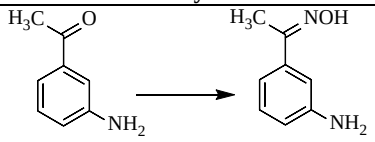
Table 1: Reaction conditions for synthesis of *p*-aminoacetanilide



88 **89**

Reaction condition	% yield	Reference
indium; acetic acid in tetrahydrofuran, heating;	100	45
hydrazine hydrate, nickel in methanol	100	46
BH_3.NMe_3, palladium hydroxide carbon in methanol, heating;	99	47
aminomethyl polystyrene resin formic acid salt, zinc in methanol,	98	48
Pd/C; Hydrazine in ethanol	98	49
Nido-decaborane; Acetic acid; palladium on activated charcoal in methanol; reduction; heating;	96	50
Ammonium ethyl polystyrene resin formate; palladium on activated charcoal in methanol	96	51
Sodium tetrahydroborate in methanol; water;	96	52
Indium; ammonium chloride in ethanol; heating;	95	53
poly-supported formate; magnesium in ethanol	95	54
hydraziniummonoformate; magnesium methanol	93	55
Zinc; Hydraziniummonoformate in water	93	56
Hydrazine hydrate; zinc in methanol	93	57
ammonium formate; magnesium in methanol	92	58
Tetrabutylammmoniumbromide; tin (II) chloride,	92	59
Iron(III) Acetylacetone; hydrazine hydrate in reflux; Chemoselective reaction;	92	60
hydrogen chloride; hydrogen; palladium on activated charcoal in ethanol; ethyl acetate	90	61
formic acid ; nickel in methanol, reduction	90	62
Ammonium formate; Reduction	90	63
Formic acid; palladium on activated charcoal in methanol	90	64
Hydrogen; hydrazine hydrate; nickel in 1, 4-dioxane	90	65
Hydrogen chloride, sodium hydroxide, Pd-C in ethanol, water, ethyl acetate	90	66
Hydrogen chloride, sodium hydroxide, Pd-C in ethanol, water, ethyl acetate	90	67
Formic acid; microwave irradiation;	90	68
Isopropyl alcohol; potassium hydroxide, microwave irradiation; chemoselective reaction;	90	69
Formic acid, nickel in methanol, Reduction	89	70
Nickel oxide; ethanol; potassium hydroxide; microwave irradiation in sealed vessel	88	71
Tellurium; ammonium chloride in methanol, reduction; heating;	85	72
polymer-CH_2NMe_2Cl; lithium methanoate; palladium in ethanol	81	73
palladium on activated carbon; hydrazine hydrate in ethanol	73	74
Hydrazine hydrate in ethanol, water	59	75
water; reduction with Bakers yeast (Saccharomyces cerevisiae);	4	76

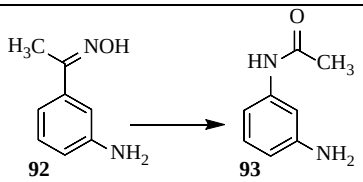
Table 2: Reaction conditions for synthesis of *m*-aminoacetanilide



90 **91**

Reaction condition	%yield	Ref
Sodium hydroxide; hydroxyl ammonium sulphate in diethyl ether, heating.	76	77
Hydroxyl amine, hydrogen chloride; sodium hydroxide in methanol, Green chemistry	68	78

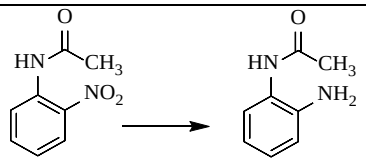
Table 3: Reaction conditions for synthesis of m-aminoacetanilide using Beckmann rearrangement



92 **93**

Reaction condition	% yield	Ref
Chloro-sulphonic acid in toluene,	98	79
propane-1, 2, 3 -tricarboxylic acid, heating	90	80

Table 3: Reaction conditions for synthesis of *o*-aminoacetanilide



94 **95**

Reaction condition	%yield	Ref
Pd/ C; hydrazine in ethanol, heating	99	81
Hydrogen; 20 $Pd(OH)_2$ on carbon in ethanol	96	82
Hydrogen; Pd in AV – 17- 8- Pd in ethanol	95	83
Hydrogen; Palladium containing anion exchanger AB -17-8-Pd in ethanol	95	84
Hydrogen; palladium on activated charcoal in ethanol.	91	85
Nickel; ammonium chloride in water, heating	91	86
Formic acid; palladium on activated charcoal in methanol, heating	90	87
Palladium 10 on activated charcoal; hydrazine hydrate in ethanol	84	88
Hydrogen; palladium on activated charcoal in methanol	80	89
Hydrogen; palladium on activated charcoal in methanol	80	90
water; acetic acid electrochemical reduction at Hg electrode, Platinum auxillary electrode	67	91
Hydrazine hydrate in ethanol, water, heating	38	92

CONCLUSIONS

In case of diamines, selective acylation of is dificult. But aminoactanilides can be prepared in good to moderate yield by vrious methods.

REFERENCES AND NOTES

1. http://intersperse.tradeindia.com/4-aminoacetanilide-412771.html,
2. http://www.chemicalbook.com/ChemicalProductProperty_EN_CB3389151.htm,
3. http://www.tcichemicals.com/eshop/en/in/commodity/A1533/,
4. Das, S.; Murugadoss, A. *p*-Aminoacetanilide mediated formation of assembly of Au nanoparticles *J. Chem.* Sci., **2008**, *120*, 547-555
5. Gaidhane, M. K.; Ghatole, A. M.; Lanjewar, K. R. Novel synthesis and antimicrobial activity of novel schiff base derived quinolin and their β-lactum derivetives *Int. J. Pharm. Pharm. Sci.*, **2013**, *5*, 421-426.
6. Kaffiji, M. J. H; Al-Anbakey, A. M. S, New Chromogenic Reagent for The Spectrophotometric Determination of Chlorpromazine HCl in Aqueous Solutions and Pharmaceutical Formulations *Int. J. Pharm. Pharm. Sci.*, **2013**, *5*, 606-611.
7. Guma, M. A Synthesis and Characterization of Acetaminophen (paracetamol)® from Acetanilide by Diazotization Reaction and Comparing with Crude. *Journal of University of anbar for Pure Sciences*, **2012**, *6*, 60-65.
8. Srivastava, A.; Singh, R. M. Vilsmeier-Haack reagent: A facile synthesis of 2-chloro-3-formylquinolines from N-arylacetamides and transformation into different functionalities, *Indian J. Chem.*, **2005**, *44*, 1868 – 1875.
9. Kalirajan, R; Jubie, S; Gowramma, B; Suresh B; Synthesis and Anesthetic Activity of Some Mannich Bases of p-Dimethylamino Benzylidene Acetanilide, *Asian J. Chem.* **2008,** *20*, 5289-5292
10. Hazelwood; Roy, J. P; Wales, N. S, *Chem. Abstr*., **1965**
11. Verma, A. K.; Martin, A; Singh, A. K. Synthesis, Characterization and evaluation of Anti-inflammatory and Analgesic activity of Benzothiazole derivatives, *Indian J. Pharm. Biol. Res*., **2014**, *2*, 84-89
12. Mulyono, Takenaka, S.; Sasano, Y.; Murakam, S., Aoki, K. Bacillus cereus strain 10-L-2 produces two arylamine N-acetyltransferases that transform 4-phenylenediamine into 4-aminoacetanilide, *Journal of Biosciences and Bioengineering*, **2007**, *103*, 147-154.
13. Idaka, E.; Ogawa, T.; Horistu, H.; Yatome, C. Degradative pathway of p-aminoazobenzene by Bacillus subtilis, *Eur. J. Appl. Microbiol. Biotech.* , **1982**, *15*, 141-143.
14. Tanaka, K.; Shimazaki, M.; Murakami, Y. Synthesis of N-Acetylbenzimidazole Derivatives *Chemical & Pharmaceutical Bulletin*, **1982**, *30*, 2714-2722.
15. Lovu, M.; Zalaru, C.; Dumitrascu, F.; Draghici, C.; Cristea, E., New substituted 2-(pyrazol-1-yl) o-, m-, p-methylacetanilides with potential local anaesthetic and antiarrhythmic action. Part I, *Il Farmaco*, **2000,** *55*, 362-368.
16. Takenaka, S.;Mulyonno; Sasano,Y.; Takahashi, Y.; Murakani, S.; Aoki, K., Microbial transformation of aniline derivatives: Regioselective biotransformation and detoxification of 2-phenylenediamine by Bacillus cereus strain PDa-1, *Journal of Bioscience and Bioengineering*, **2006,** *102*, 21-27
17. Fang, Z-Y; Jiang, H.; Ye, X-D. Synthesis and fungicidal activity of pyrazolecarboxamide containing α-aminoacetanilide moiety *E-Journal of Chemistry*, **2012**, *9*, 211-218.
18. a) Erdtmen; Lofgren; *Svensk Kemisk Tidskrift*., **1937,** 163-171. b) Ahmed, et al.: *Journal of the Indian Chemical Society*, **1938**, *15*, 152-159, (*Chemical Abstracts*, **1938**, *32*, 7040).
19. Haga, T.; Nagano, E.; Stao, R.; Morita, K, Benzotriazoles, and their production and use 1988, US4755215 A
20. Yanxi, S. A Study on the Synthesis of p - Aminoacetanilide Dyestuff Industry; **2001**, *38*; 42-43
21. Hou, L. H; Wang, J.; Hai, Y. L en.cnki.com.cn/article _en/CJFDTOTAL-GONG20090.htm.

22. Zupei, B. L; Wei, C; Shandong; Qingdao . A green-Study on the Synthesis of p-Aminoacetanilide *Chemical Industry Times*;**2004,** 4..
23. George, F. D; Nuclearly halogenated dialkenylaminoacetanilides 1968, US3412152 A
24. Li, H. J; Shang, M. X. en.cnki.dom.cn/article_en/CJFDTOTAL-HXSS200705009.htm
25. Ghaemy, M.; Barghamadi, M. Fluorene-ring-containing diamine and resultant soluble thermally stable polyamides, *J. Appl. Polym. Sci.*, **2008**, *110*, 1730-1738
26. Dahlbom, R.; Tegner, C.; Willman, N.A. Further Studies on Amino Esters of Substituted Phenylcarbamic Acids. *Acta Chem.Scand.* **1957,** *11*, 1350-1354.
27. Lingala, S.; Nerella, R.; Poudala, K. Synthesis and evaluation of new 2-Chloro-N-[(Z)-(2-oxo-5 sulfamoyl -indolin-3-ylidene) amino] acetamide derivatives for their antimicrobial and anti- inflammatory activity *Pharmanest*, **2013**, *4*, 1152-1161
28. Chettur, G.; Benkovic, S.J., A new chemical synthesis of 2-amino-(N-d-ribofuranosyl)acetamide 5′-phosphate, *Carbohydr Res.* **1977**, *56*, 75-86
29. Fosdick, L.S.; Rapp, G.W, Some Derivatives of Acetanilide1a, *J. Am. Chem. Soc.* **1943**, *65*, 2307-2308
30. Haga, T.; Nagano, E.; Stao, R.; Morita, K., Benzotriazoles, and their production and use **1988**, US4755215 A
31. Zupei, L.; Wei, C., en.cnki.com.cn/Article_en/CJFDTOTAL-HGJS200404022.htm
32. Yanxi, S.; Jiging, Y., en.cnki.com.cn/Article_en/CJFDTOTAL-GONG200106015.htm
33. Zhang, L.R.; Zhang, Z-Xia, en.cnki.com.cn/Article _en/CJFDTOTAL–GONG200304017.htm
34. Xiao-Zhi, L.; Shi-wei, L.; en.cnki.com.cn/Article_en/ CJFDTOTAL–GONG200306014.htm
35. Wen, L., en.cnki.com.cn/Article_en/CJFDTOTAL–GONG20050 3014.htm
36. Jian, G., en.cnki.com.cn/Article_en/CJFDTOTAL–CHUA19840 4014.htm
37. Hao, L.; Rouy, L., en.cnki.com.cn/Article_ en/CJFDTOTAL–CH UA20090 7 006.htm
38. Ramann; Rajasekaran, K; Sakthivel, A. *Indian J. Chem. Soc*., **2007**, *84*, 117-121
39. Hai-yam, X.; Jing, H.N, en.cnki.com.cn/article_en/CJFDTOTAL-HNHG201003018.htm
40. Raj, K.K.; Sargal, G.; Fungicidal activities of Co(II), Ni(II) and Cu(II) complexes with Schiff`s bases *Int. J. Chem.*,**2012**, 1680-1686
41. Wang, D.; Cai, Q.; Ding, K., An Efficient Copper-Catalyzed Amination of Aryl Halides by Aqueous Ammonia, *Adv. Synth. Catal.*, **2009**, *351*, 1722-1726
42. Harris, M. C.; Huang, X.; Buchwald, S. L. Improved Functional Group Compatibility in the Palladium-Catalyzed Synthesis of Aryl Amines *Org. Lett.* **2002**, *4*, 2885-2888.
43. Cheung C. Wai, Surry, D. S., and Buchwald, S. L.,Mild and Highly Selective Palladium-Catalyzed Monoarylation of Ammonia Enabled by the Use of Bulky Biarylphosphine Ligands and Palladacycle Precatalysts, *Org. Lett.*, **2013**, *15, 3734 - 3737.*
44. Pitts Michael R., Justin R. Harrison and Christopher J. Moody, Indium metal as a reducing agent in organic synthesis, *J. Chem. Soc., Perkin Transactions***, 2001**, *1***,** 955 – 977.
45. Lue, L.; Chen, J.; Ling, W.; Li, L.; Xian, C.; Wang, H.; Wang, G.; Wang, Y, 2-pyrimidinyloxy-N-aryl-benzylamine derivatives, their processes and uses US2003/220198 A1**,** 2003
46. Couturier, M.; Tucker, J. L; Andresen, B. M.; Dube, P; Brenek, S. J.; Negri, J. T, Palladium catalyzed activation of borane–amine adducts: rate enhancement of amine–borane methanolysis in the reduction of nitrobenzenes to anilines, *Tetrahedron Lett.*, **2001**, *42*, 2285-2288
47. Srinivasa, G. R.; Abiraj, K.; Gowda, D. C.; Polymer-supported formate and zinc: A novel system for the transfer hydrogenation of aromatic nitro compounds, *Indian J. Chem. Sec. B Organic and Medicinal Chemistry*, **2006**, *45B*, 297-301
48. dos Santos, C. M., McCabe, T., Watson, G. W., Kruger, P. E., Gunnlaugsson, T. The Recognition and Sensing of Anions through "Positive Allosteric Effects" Using Simple Urea−Amide Receptors, *J. Org. Chem.*, **2008**, *73*, 9235-9244
49. Bae, J.W; Cho, Y.J; Lee, S.H; Yoon, C.M, Chemoselective reduction of nitroaromatics to anilines using decaborane in methanol, *Tetrahedron Lett.* , **2000**, *41***,** 175-177.
50. Abiraja K., Srinivasaa G. R. & Gowdaa D. C., Transfer Hydrogenation of Aromatic Nitro Compounds Using Polymer-Supported Formate and Pd-C, *Synth. Comm.*, **2007**, *35*, 223-230
51. Shil, A.K.; Sharma, D; Guha, N.R; Das, P Solid supported Pd(0): an efficient recyclable heterogeneous catalyst for chemoselective reduction of nitroarenes, *Tetrahedron Lett.*, **2012**, 53, 4858-4861
52. Moody, C.J; Pits, M.R, Indium as a Reducing Agent: Reduction of Aromatic Nitro Groups, *Syn lett*, **1998**, *9*, 1028-1028
53. Abiraj K., Srinivasa G. R. and Gowda D. C., Simple and Efficient Reduction of Aromatic Nitro Compounds using Recyclable Polymer-Supported Formate and Magnesium, *Aust. J. Chem.*, **2005**, *58*, 149-151
54. Gowda, S , Gowda, D.C Application of Hydrazinium Monoformate as New Hydrogen Donor with Raney Nickel; A Facile Reduction of Nitro and Nitrile Moieties, *Tetrahedron*, **2002**, *58*, 2211-2213
55. Gowda, S; Gowda, D.C; Kempe, B.K, Hydrazinium Monoformate: A New Hydrogen Donor. Selective Reduction of Nitrocompounds Catalysed by Commercial Zinc Dust*Synth. Comm.*, **2003**, *33*, 281-289
56. Gowda, S; Gowda, D.C, Zinc/Hydrazine: A Low Cost- Facile System for the Reduction of Nitrocompounds, *Indian J. Chem. Sec.- B Organic and Medicinal Chemistry*, **2003**, *42*, 180-183
57. Srinivasa, G. R.; Abiraj, K.; Gowda, D. C., Magnesium/ Ammonium Formate : A Cost-Effective System for the Rapid and Selective Reduction of Nitro Compounds, *Indian J. Chem.- Sec. B Organic and Medicinal Chemistry*, **2003**, *42*, 2882-2884
58. De, P; Efficient Reductions of Nitroarenes with $SnCl_2$ in Ionic Liquid, *Synlett*, **2004**, *10*, 1835-1837
59. Cantillo, D.; M.M, Moghaddam; Kappe, C.O , Hydrazine-mediated Reduction of Nitro and Azide Functionalities Catalyzed by Highly Active and Reusable Magnetic Iron Oxide Nanocrystals, *J. Org. Chem.*, **2013**, *78*, 4530-4542
60. Sternfeld, F; Baker, R; Broughton, H.B., Guiblin, Alexander R., Jelley, Richard A., Matassa, Victor G., Stanton, Joshephine A., Beer, Margaret S., Stanton, Joshphine A., Hargreaves, Richard J., Shepheard, Sara L., Longmore, Jeanette, Razzaque, Zerin, Graham, Micheal I., Sohal, Bindi, Street, Leslie J *Bioinorg. Med. Chem. Lett.*, **1996**, *6*, 1825-1830
61. Gowda D.C., Gowda A.S. P; Baba R; Gowda, S, Nickel-Catalysed Formic Acid Reductions, A Selective Method for the Reduction of Nitro Compounds, *Synth. Comm.*, **2000,** *30*, 2889-2895
62. Gowda D.C.; Mahesh, B; Catalytic Transfer Hydrogenation of Aromatic Nitro Compounds by Employing Ammonium Formate and 5% Platinum on Carbon, *Synth. Comm.*, **2000**, *30*, 3639-3644
63. Channe D.C.; Gowda S, Formic Acid with 10% Palladium on Carbon: A Reagent for Selective Reduction of Aromatic Nitro Compounds, *Indian J. Chem. Sec.-B Organic and Medicinal Chemistry*, **2000**, *39*, 709-711
64. Dzierzbicka K., Trzonkowski P., Sewerynek P. and Myśliwski A., Synthesis and Cytotoxic Activity of Conjugates of Muramyl and Normuramyl Dipeptides with Batracylin Derivatives, *J. Med. Chem.*, **2003**, *46*, 978-986
65. Baker et al., 4-substituted 1,2,4-triazole derivatives **1996,** US5554629 A1
66. Baker et al., Azetidine, pyrrolidine and piperidine derivatives **1998** US5854268 A1
67. Arya, K; Dandia, A, Selective Reduction of Nitro Compounds Using CeY Zeolite Under Microwaves, Korean *J. Chem. Soc.*, **2010**, *54*, 55-58
68. Farhadi, S; Siadatnasab, F; Kazem, M Microwave-assisted rapid and efficient reduction of aromatic nitro compounds to amines with propan-2-ol over nanosized perovskite-type SmFeO3 powder as a new recyclable heterogeneous catalyst *J. chem. Res.*, **2011**, *35*, 104-108
69. Channe G; Gowda, P; Baba, R; Gowda, S, Nickel-Catalyzed Formic Acid Reductions. A Selective Method for the Reduction of Nitro Compounds *Synth. Comm.*, **2000**, *30*, 2889-2895
70. Farhadi, S; Kazem, M; Siadatnasab, F NiO nanoparticles prepared via thermal decomposition of the bis(dimethylglyoximato) nickel(II) complex: A novel reusable heterogeneous catalyst for fast and efficient microwave-assisted reduction of nitroarenes with ethanol *Polyhedron*, **2011**, *30*, 606-613

71. Khan, R. H. Tellurium mediated reduction of aromatic nitro groups *J. chem. Res.-part-S*, **2000**, 290-291
72. Solodenko, W; Wen, H., Leue, S., Stuhlmann, F.; Sourkouni-Argirusi, G.; Jas, G.l Schoenfeld, H.; Kunz, U.; Kirschining, A. *Eur. J. Org. Chem.*, **2004,** 3601-3610
73. Boyle, E. M., McCabe, T; Gunnlaugsson, T. Synthesis, photophysical and NMR evaluations of thiourea-based anion receptors possessing an acetamide moiety *Supramolecular chemistry*, **2010**, *22*, 586-597
74. Deka, D., Chandra, K., Hari, S. Selective reduction of aromatic nitro groups in the presence of amide functionality *J. chem. Res.*, **2006**, 223-234
75. Takeshita, M; Y.S; Kiya, Rieko, Higuchi, Naoko, Kobayashi, Yumi, Reduction of aromatic nitro compounds with baker's yeast, *Chem. Pharm. Bull.*, **1989**, *37*, 615-617
76. Witek, S.; Bielawski, J.; Bielawska, A. New pesticides and intermediates. Part vii. Some azaalkenyl derivatives of N-phenylurea and N-phenylcarbamic acid *Polish J. Chem.*, **1981**, *55*, 2589 – 2600.
77. Aakeroey, C. B.; Sinha A. S., Synthesis of ketoximes via a solvent-assisted and robust mechanochemical pathway, *RSC Adv.*, **2013**, *3*, 8168 – 8171.
78. Li D.; Shi F.; Guo S.; Youquan D. Highly efficient Beckmann rearrangement and dehydration of oximes, *Tetrahedron Lett.*, **2005**, *46*, 671 – 674.
79. Thopate; Ramchandra; S.; Kote, S.; Rohokale, S.V.; Thorat, N. M. Citric acid catalysed Beckmann rearrangement, under solvent free conditions *J. Chem. Res.*, **2011**, *35*, 124 – 125.
80. Dos Santos Cidália M. G., M Thomas, Watson G. W., Kruger P. E. and Gunnlaugsson T., The Recognition and Sensing of Anions through "Positive Allosteric Effects" Using Simple Urea−Amide Receptors, *J. Org. Chem.*, **2008**, *73*, 9235 – 9244.
81. Sadhu C., Dick K., Treiberg J., Sowell C. G., Kesicki E.A., [illegible]er A., Inhibitors of human phosphatidylinositol 3-kinase delta**,** *ICOS Corporation***, 2003,** US6667300 B2, 98
82. Abdullaev; Nasibulin; Klyuev Hydrogenation of ortho-substituted nitrobenzene over AV-17-8 Palladium containing ion exchanger *Russ. J. org. Chem.*, **1997**, *33*, 1676 – 1677.
83. Klyuev; M. V.; Volkova, T. G.; Abdullaev, M. G. Hydrogenation of ortho-Substituted Nitrobenzenes over Palladium Catalysts *Petrol. Chem.*, **2002**, *42*, 30 – 33.
84. Fonseca, T.; Gigante, B.; Gilchrist, Thomas L, A short synthesis of phenanthro[2,3-d]imidazoles from dehydroabietic acid. Application of the methodology as a convenient route to benzimidazoles, *Tetrahedron*, **2001**, *57*, 1793 – 1799.
85. Bhaumik, K.; Akamanchi K.G.; Nitroarene reduction using Raney nickel alloy with ammonium chloride in water, Canadian *J. Chem.*, **2003**, *81*, 197 –198.
86. Gowda, D C., Gowda, S. Formic acid with 10% palladium on carbon: A reagent for selective reduction of aromatic nitro compounds, *Indian J. Chem. Section- B Organic and Medicinal Chemistry*, **2000**, *39*, 709 – 711.
87. Boyle, E. M., McCabe, T, Gunnlaugsson, T. Synthesis, photophysical and NMR evaluations of thiourea-based anion receptors possessing an acetamide moiety *Supramolecular Chemistry*, **2010**, *22*, 586-597
88. Shepherd, T.; Smith, D. M. o-Nitrobenzylidene compounds. Part 4. The cyanide-induced cyclisation of o-acetamido-N-(o-nitrobenzylidene)anilines: an improved route to quinoxalino[2,3-c]cinnolines *J. chem. Soc., Perkin transactions 1: Organic and Bio-organic chemistry*, **1987**, 501-506.
89. Matrinez, M.; Francisco, J.; Leon, R.; Jose, L.; Padilla, M.; Itazia, I., Rosales, H.; Maria J.; Contreras, R. *Phosphorous, sulfur and silicon and the related elements*, **1996,** *115*, 217-226.
90. Alberti, A.; Carloni, P.; Greci, L.; Stipa, P., Andruzzi, R. Chemical and electrochemical reduction of ortho-nitroanilides. A combined chemical, polarographic and EPR study *J .chem. Soc., Perkin Transcations 2: Physical Organic Chemistry*, **1991**, 1019-1023.
91. Deka, D.; Chandra, K.; Hari, S. Selective reduction of aromatic nitro groups in the presence of amide functionality *J. chem. Res.*, **2006**, 223-224.
92. Takeshita, M.; Yoshida, S.; Kiya, R.; Higuchi, N.; Kobayashi, Y. Reduction of aromatic nitro compound with baker's yeast, *Chem. Pharm. Bull.*, **1989**, *37*, 615-617.