Available online at www.jcsonline.in
Journal of Current Science & Humanities 9 (3), 2021, 1-05.
Impact Factor- 2.05

Reduction of aromatic and hetero aromatic zo compounds with hydrazine hydrate

Mr S.Khaja Shamshuddin[1], Mrs. Azmatunnisa Esmat[2], Mrs. Koppula Ramya Sree[3]

Assistant professor[1,2,3]

Department of Pharmaceutics,

Global College of Pharmacy, Hyderabad. Chilkur (V), Moinabad (M), Telangana- 501504.

ABSTRACT: Hydrazine hydrate, either with or without a catalyst, has reduced the azo compounds. When it comes to reducing azo functional groups to get new amines, this reaction is an appealing alternative.Using hydrazine hydrate, the authors of this review describe the reduction of faromatic or heteroaromatic azo compounds.

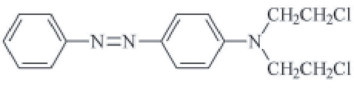
KEYWORDS: Reduction,azocompounds,uncatalyzedreduction,hydrazinehydrate

1. INTRODUCTION

The aminogroup provides a platform for further derivatization, making the reduction of azo compounds to amines a valuable chemical process in synthetic organic chemistry. Many drugs, polymers, photographic materials, dyes, and pigments rely on amines in their manufacture as well. Reduction of azo(4,5,6) or reduction of faromatic nitro(1,2,3) compounds often yields the principal aromatic amines. It is usual practice to employ hydrazinehydrate to reduce nitro groups when catalysts are present (7,8).Additionally, azo compound reductions using hydrazine hydrate in the presence of a catalyst have been carried out (9,10).The conversion of azo-arenes to aminoarenes with hydrazinehydrate in the presence of aluminum powder in ethanol was established by Pasha and Nanjundas-wany (11). With the use of hydrazinehydrate without a catalyst, Ergenç and Rollas (Açıkkol) (12-21) have been doing azo compound reductions since 1972.Hydrazinehydrate reduces the azo derivative, as shown by Ross and Warwick (22).But we haven't isolated reduction products in our investigation. All things considered, the first writers to record the reduction-tive cleavage of azo compounds to provide the corresponding amines without a catalyst were Ergenç and Rollas. The reduction of azo compounds utilizing hydrazine hydrate without a catalyst has been reported by Koppesetal.(25), Zhang and Wang (23), and Pasha and Nanjundas- wamy (24). Rollas used hydrazinehydrate as a catalyst-free synthesis method to produce specific aminophenyl modified 1,2,4-triazoles and 1,3,4-thiadiazoles from their corresponding azo compounds (26, 27). This review will focus on the reductive cleavage of azo compounds with hydrazine hydrate as well as the reducing characteristics of hydrazine hydrate.

2. THE REDUCTION OF AZO COMPOUNDS USING HYDRAZINE HYDRATE WITHOUT CATALYST

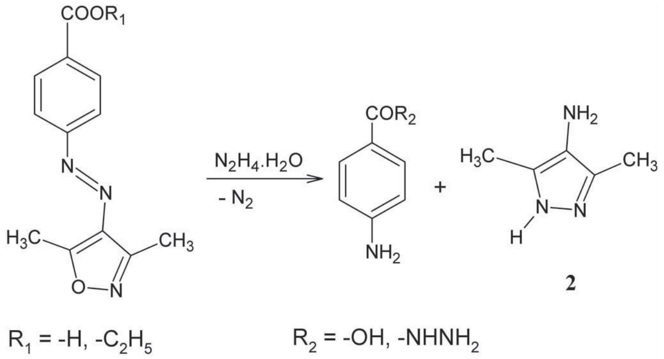
Hydrazine hydrate is a strongreducing agent.Generally, it has been used the reduction of nitrogroup(28).Inthereductionoftheazocompoundswith hydrazine hydrate, Raney nickel has beenused as a catalyst (9, 29). In 1955, Ross and Warwick(22)showedthattheazoderivativescouldbereduced by hydrazine hydrate. They reported thetumour-growth inhibitory activity of azo-derivativesofaromaticnitrogenmustardsandthereduc-tion of azo-linkage with hydrazine hydrate to cor-relate the ease of reduction of N,N-bis(2-chloroe-thyl)-4-(phenyldiazenyl)aniline(**1**)withitsbiolog-ical activity. Therefore the substituted derivativesof **1** have been prepared. Of the reducing agentsexamined, the most consistent results were obtained using hydrazine hydrate. However in thisresearch, the reduction products, hydrazo-com-pounds or amines, have not been isolated.



1

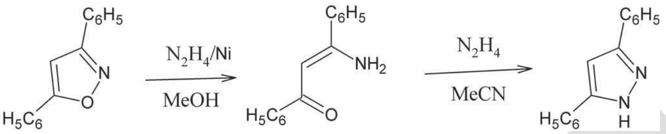
FIGURE1.N,N-bis(2-chloroethyl)-4-(phenyldiazenyl)aniline.

In 1972, Ergenç and Açıkkol (Rollas) (12) published the first report of the reductive cleavage of azo compounds withhydrazinehydratewithoutacatalystforthesynthesisof4-amino-3,5-dimethylpyrazole**2**.Inthisreaction,isoxazoleringwas observedtobeconvertedtopyrazoleringwhiletheazofunc- tion is reduced to amino group.(Scheme 1).



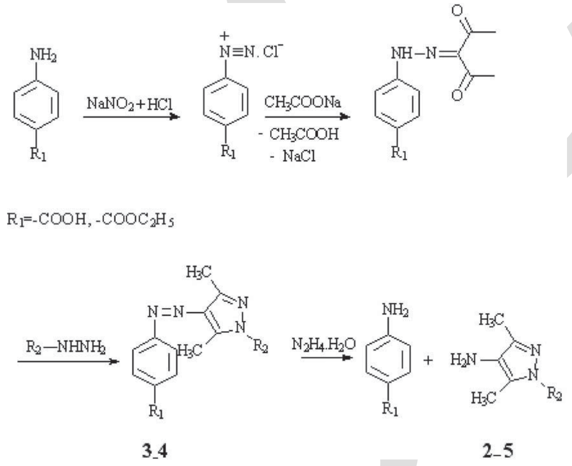
SCHEME1. Thereductionofazoisoxazoleswithhydrazinehydrate.

Also, Sviridov et al. (30) reported the transformation of the isoxazole into the pyrazole with hydrazine hydrate in the presence of Raney nickel catalyst (Scheme 2).



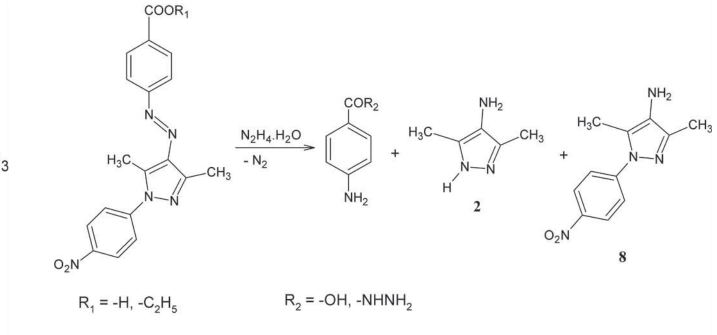
SCHEME2. Theconversionof3,5-diphenylisoxazoleto3,5-diphenylpyrazole.

A method developed by Rollas (31) for the synthesis of substituted amines from the corresponding heteroaromatic azo compounds. Aryldiazonium salts can be coupled with activealiphatic CH compounds. Therefore the aryldiazonium saltswere coupled with acetylacetone and the obtained hydrazones,which are stable form of the coupling products, were cond-enced with hydrazine or substituted hydrazines to form azo-pyrazoles. These azopyrazoles were heated with an excessamount of hydrazine in ethanolic solution on a steam bath un-til red or orange colour of the solution changed into pale yel-low and also until nitrogen no longer evolved.



SCHEME3. Thereductionofazopyrazoleswithhydrazinehydrate.

Thereductivecleavageof**3**and**4**withhydrazinegave4-amino-3,5-dimethylpyrazole **2**and the other amines, 4-aminobenzoicacidor4-aminobenzoicacidhydrazide.Intheexperimentalconditionstheestergrouphavealsobeenconvertedtohydrazide. Thereduction of nitro group-containing azo compound, 3,5-dimethyl-4-(4-ethoxycarbonyl-phenylazo)-1-(4-nitrophenyl) pyrazole**7**, with hydrazine hydrate in ethanol withoutacatalystispresentedinScheme4.Thecarbon-nitrogen bond has also been reduced (14, 31).

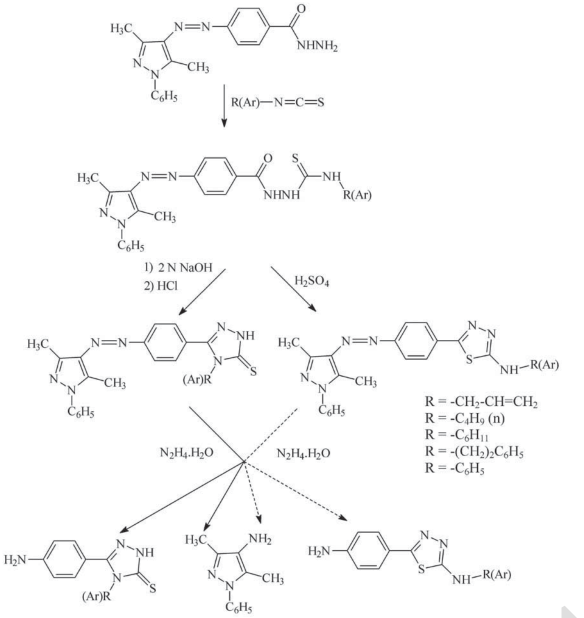


6-7

SCHEME4. Thereductionofazopyrazolesbearingnitrogroup.

Recently, Rollas et al. (21) developed a new method for the synthesisof4-amino-3,5-dimethylpyrazole.Anilinewasused as the starting material instead of 4-aminobenzoic acid or ethyl 4-aminobenzoate. The reduction of the corresponding azo compound was affordedby lower amounts of hydrazine hydrate at room temperature. In this method, the separation of amines had been found easier than first method. Aniline was removed by extraction with diethyl ether. Since the reaction timewasverylong,thereductionofazocompoundswascarriedoutwithhydrazinehydrate(1:3)byrefluxinginethanol for30mintosynthesize4-amino-3,5-dimethylpyrazole(Rollas,unpublisheddata).Presenceofexcesshydrazinehydrate have been found unnecessaryfor the reduction.

The uncatalyzed reduction with hydrazine hydrate was applied to reduce different azo compounds containing 1,2,4-triazolin-5-thione and 1,3,4-thiadiazole rings by Rollas (32, 33).The synthetic pathway of the starting compounds which wereobtained from the corresponding thiosemicarbazide derivatives(34)andtarget1,2,4-triazolin-5-thiones**9-13**and1,3,4-thiadiazoles**14-18** (26,27)arepresentedinScheme5.

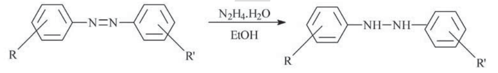


9 - 13 **5** **14 - 18**

R= $-CH_2CH_2CH_3$

SCHEME5. The reduction of azotriazoles and azothiadiazoles with hydrazine hydrate.

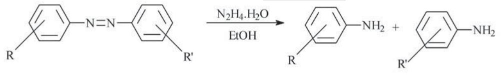
ZhangandWang(23)reportedthesynthesisofcertainhydrazo compounds starting from the azobenzene, substituted symmetric or nonsymmetric azobenzeneswith the use of hydrazine hydrate in ethanol (Scheme 6).



R	H	4-CH_3	4-Cl	4-OCH_3	4-Br	3,4-CH_3	4-F	4-Cl	4-Br	4-CH_3	3-Cl	4-NO
R’	H	4’-CH_3	4’-Cl	H	4’-Br	3’,4’-CH_3	H	H	H	H	H	H

SCHEME 6. Thereductionofdiazobenzenestohydrazocompoundswithhydrazinehydrate.

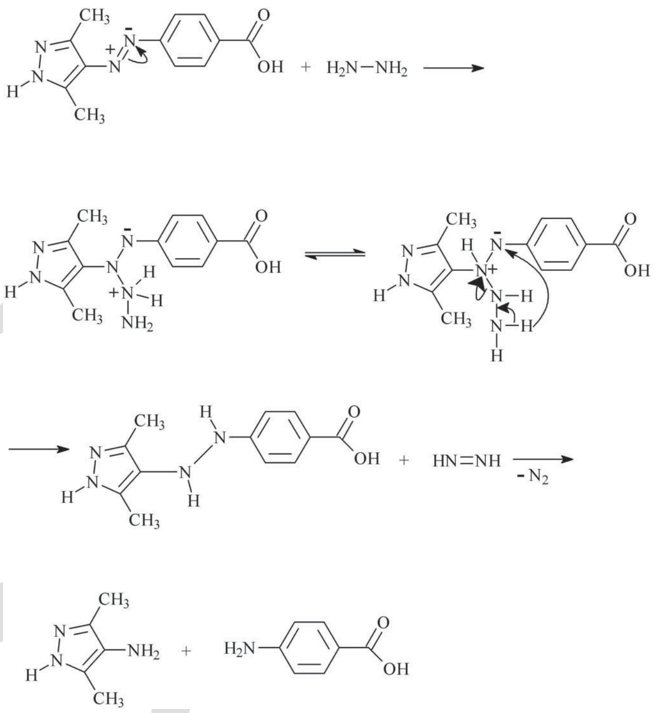
Pasha and Nanjundaswamy (24) describedthe synthesis ofcertain aromatic amines from the corresponding azoareneswith excess hydrazine hydrate without a catalyst in refluxingethanol similar to Rollas’s procedure (26, 27, 31).



R	H	2-CH_3	3-CH_3	3-OCH_3	2-OH	2-Cl	2-OH	2-COOH	4-COOH	4-NH_2
R’	H	2’-CH_3	3’-CH_3	3’-OCH_3	2’OH	2’-Cl	H	4’-$N(CH_3)_2$	H	H

SCHEME7. Thereductionofdiazobenzenestoamineswithhydrazinehydrate.

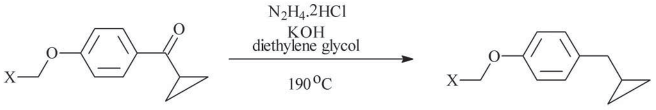
Scheme8 shows a proposed method for the catalyst-free reduction of azo groups by hydrazine hydrate.Koppesetal may provide evidence that supports the stated idea.The researchers found that diimide was effective in reducing azo compounds.Theproductionof diimide from hydrazine hydrate could be obtained by an oxi- dant agent. Diimide could be produced by air oxygen. How- ever Koppes et al. also reduced azo compounds to hydrazo compoundsinanaerobicconditionsbyprotectingfromtheair oxidation.Inthehydrazinehydratereduction,azogroupmay actasanoxidant.AccordingtotheprocedurereportedbyKo- ppes et al., the minumum amount of hydrazin hydrate was usedtherefore,azocompoundswereonlyreducedtohydrazo compounds and the further reduction hasnot been occured. We thought that the mechanism of reduction is unclear.



SCHEME 8. Theproposedmechanismofthereductionofazocompoundswith hydrazinehydrate.

3. OTHERREDUCTIONSWITHHYDRAZINE HYDRATE

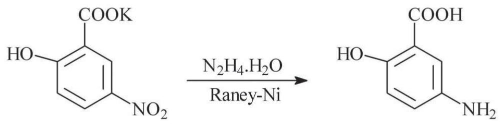
Hydrazine hydrate has been usedin the reduction of ketones.The Wolff-Kishner reduction is usually carried out by heatingthe ketone with hydrazine and alkali. In this procedure, hydrazoneisnotisolated.Themechanismofreductioninvolvesbase-catalyzed tautomerization of the hydrazone followed byloss of nitrogen. Dwivedi et al. (35) used phenyl cyclopropylketones as starting material for the reduction ofketones tomethylene groups (Scheme 9).



SCHEME 9. Thereductionofcyclopropylketoneswithhydrazinehydrate(Wolff-Kishnerreduction)

Many amines have been prepared by the reduction of correspondingnitrocompounds.Alargenumberofreducingagents have been used for the eduction of nitro group. One ofthe goodreducingagentsishydrazinehydratethathasbeenused in the presence of heterogeneous catalyst. Vass et al. (36) described solvent-free reduction of aromatic nitro compoundswith hydrazine hydrate supported on solid material, alumina,in the presence of $FeCl_3.6H_2O$ under microwave irradiation.Kumbhar et al. (37) reduced aromatic nitro compounds withhydrazine hydrate in the presence of oxide-MgO catalyst pre-pared from a Mg-Fe hydrotalcite precursor. It is reported thatthe catalyst was found to be highly active and selective.

Breviglieri et al. (38) reported the reduction of 5-nitrosalicylicacid potassium salt **19** to 5-aminosalicylic acid **20** with hydra-zine hydrate in the presence of Raney nickel that has been usedas a catalyst with hydrogen donor hydrazine.



19 **20**

FIGURE 2. Thereductionof5-nitrosalicylicacidpotassiumsaltto5-aminosali- cylic acid with hydrazine hydrate

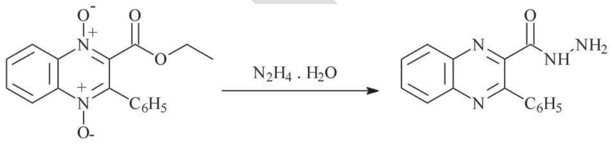
Gowda S. and Gowda D.C. (39) reported the reduction of aliphaticandaromaticnitrocompoundsandnitrilestocorresponding amines in the presence of Raney nickel and hydrazinium monoformate. The application of hydrazinium monohydrate/Raney nickel is a new system of the reduction of nitro and nitrile groups (Scheme 10). Majid et al. (40) re-portedthereductionofanintermediatenitrosocompoundto amine by hydrazine hydrate without a catalyst.

$$R-NO_2 \xrightarrow[\text{Raney Ni / }CH_3OH]{N_2H_4\ .\ HCOOH} R-NH_2$$

$$R-CN \xrightarrow[\text{Raney Ni / }CH_3OH]{N_2H_4\ .\ HCOOH} R-CH_2-NH_2$$

SCHEME10. Thereductionofnitroandnitrilegroups.

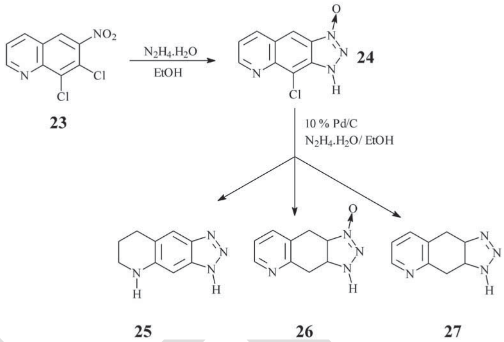
Lima et al. (41) reported the reduction of ethyl3-phenylquinoxaline-2-carboxylate 1,4-di-N-oxide**21**to 3-phenyl-2-quinoxalinecarbohydrazide **22**with hydrazine hydrate.



21 **22**

FIGURE3. Thereductionofethyl3-phenylquinoxaline-2-carboxylate1,4-di-N- oxide.

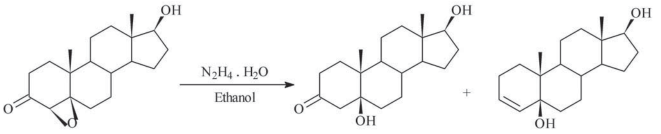
Carta and Paglietti (42) reported the synthesis of compound **24** starting from **23** in the presence of excess hydrazine hydrate in ethanol.Inthefurtherreductionof**24**,whilethechlorineand N-oxidereducedbyhydrazinehydrateandPd/Ccatalyst,pyridineandbenzeneringsofquinoxalinereducedtodihydroor tetrahydro products **25-27**.



SCHEME11. ThereductionofchlorineandN-oxidebyhydrazinehydrate.

An essential step in organic synthesis for the synthesis of novel compounds is the reduction of carbon-carbon double bonds. Additionally, hydrazine hydrate has been used to reduce double bonds via a diimid (HN=NH) intermediate (43). In addition to compounds 9 and 14, which also include reducedallyl groups, Rollas's technique (26,27) also yielded the reduced azo products (Scheme 5). Diimide has been synthesized from hydrazine hydrate in the presence of an azo group or oxygen in the air. The result is the reduction of the allyl group to the propyl group. The reduction of the allyl group to propyl does not occur in the presence of modest amounts of hy-drazine hydrate, according to Rollas's modified reduction process (unpublished results). Amines were produced by reducing the azo group.

An essential step in the structural elution of natural compounds is the reduction of α, β-epoxy ketones to their corresponding β-hydroxy ketones.In moderate circumstances, utilizing hydrazine hydrate in a thiol (Scheme 12), Salvador et al. (44) obtained β-hydroxyketones by reductive cleavage of the steroidal epoxy ketones.



SCHEME 12. The reduction of □ ,□-epoxy ketones to the corresponding □-hydroxyketones.

4. CONCLUSION

Various techniques for the synthesis of aromatic or heteroaromatic primary amines have been taught, and the reduction reaction that is generated by using hydrazine hydroxide with or without a catalyst has been covered. One benefit of the suggested approach is that it allows for the preparation of primary amines with excellent yields.The uncatalyzed reductive cleavage of azo compounds with hydrazinehydrate is the primary subject of this review..

REFERENCES

1. In Walsh's Textbook of Practical Organic Chemistry (Wiley: New York, 1989, pp. 891), the authors list Furniss, Hannaford, Smith, and Tatchell.

Chohapatra SK, Sonavane SU, Jayaram RV, and Selvam P. Mesoporous aluminophosphate moleculer sieves replaced with cobalt (II) undergo heterogeneous catalytic transfer hydrogenation of aromatic nitro and carbonyl compounds. Journal of Tetrahedron Physics, 43, 8527–8529 (2002).

3. Gupta R.K., Sudheer CH, Dash J, Khan FA. Using zinc and ammonium salts for the chemo-selective reduction of aromatic nitro and azo compounds in ionic liquids. Chapter 44: 7783–7787, Tetrahedron Letters, 2003.

Yus M., Alonso F., and Radivoy G. Using the Ni-Cl2.2H2O-Li-DTBB (cat.) combination, hydrazine, azo and azoxy compounds, and amine N-oxides are reduced.The Tetrahedron, volume 56, pages 8673–8678, 2000.

5. The authors are Mohapatra SK, Sonavane SU, Jayaram RV, and Selvam P. Mesoporous aluminophosphate molecular sieves with trivalent iron incorporation undergo reductive cleavage of azo dyes and nitroarenes. Chapter 46: 155–163, Applied Catalysis in the Environment, 2003.

Sixth, Selvam P, Mohapatra SK, Jayaram RV, Sonavane SU. On the other hand, the simultaneous hydrodehalogenation and reduction of substituted arylhalides over PdMCM-41 catalyst transfer hydrogen conditions, as well as the selective reduction of alkenes, α,β-unsaturated carbonyl compounds, nitroarenes, nitroso compounds, and N,N-hydrogenolysis of azohydrazo functions, are all possible.—2004, Tetrahedron Letters 45: 3071–3075.

(7) Lauwiner, Roth, and Rys.Using an iron oxide/hydroxide catalyst, hydrazine hydrate is used to reduce aromatic nitro compounds. III. Nitrogroup selective reduction in aromatic azo compounds.The article was published in 1999 in the journal Applied Catalysis A and ran on the pages 9–14.

Kumaraja M. and Pitchumani. 8. A straightforward and effective method for reducing nitroarenes using flaujasite zeolites was published in 2004 in the journal Appliqué Catalysis A, 265: 135-139.

Personnert WH, Los M, and Thomson N. Hydrozine reduction of azo compounds. Scientific American, 1277, 1956. Volume 51, Issue 6636a, 1957.

10. Abiraj K., Gowda S., and Gowda DC. The Raney nickel and ammonium formate/formic acid method allows for the rapid cleavage of azo compounds to amines. Native American Journal of Chemical Section B-Organic Chemistry, Inc. Medical Chemistry, 42: 1774-1776, 2003.

Phasesa MA, Nanjundaswamy HM. 11. Conversion of azoarenes to aminoarenes using aluminohydrazine hydrogenation and reductive fission. The Journal of Chemical Research, volume 7, pages 752-752, 2004.

Twelve, Ergenç and Açıkkol. Two novel compounds that are azoisoxazoles. The publication was published in 1972 in the Journal of Pharmaceutical Sciences in Istanbul, volume 8, pages 108-162.

13. (Acethylacetonilidenhidyrazono) ErgençN, RollasS.p.