16 Synthesis and Characterization of Diazohydroxyamine

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Abstract

Diazohydroxyamines (DHA) or Ammelines are well known analytical reagents for many transitions and a few non transition metals. The compounds have been recycled as spectrophotometric and complexometric substances for metal determination. A number of Ammelines have also been investigated for their biological properties, including antibacterial, antifungal, insecticidal, coiled healing, anti-inflammatory, and anti-tubercular properties.

Keywords: DHA, Ammelines, Antibacterial, Antifungal, Insecticidal.

Introduction

Spectrophotometry is an excellent tool for determination of several transition metals. Heavy metals are commonly determined using UV–VIS spectrophotometry and often utilize a metal-complex formation reaction with some chromogenic reagents and is becoming standard in several laboratories because it offers easy, modest and rapid resolve in low to high concentrations at reduced cost. Generally analytical chemistry related to metal complexes is based on the synthesis of specific reagents. In this context, many organic reagents, due to their complexing ability and chelating nature are capable for complexation of metal ions. On the basis of reactivity it is found that -OH, -SH and -NO containing compounds are used as good organic reagents. Literature survey reveal that a large number of Ammelines find application as spectrophotometric analytical reagents, They show good complexing ability with transition metal and non- transition metal and it was firstly examined by Elkins and Hunter.

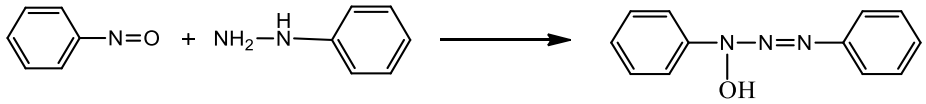
General Method for DHA Synthesis

Three synthetic methods are available for the preparation of Ammelines.

- **First Method**

It is the first method, reported by Bamberger et al, Gebhard and Thompson et al and Fischer et al. This synthesis shows nitrobenzene and substituted nitrobenzene reduction with phenyl hydrazines.

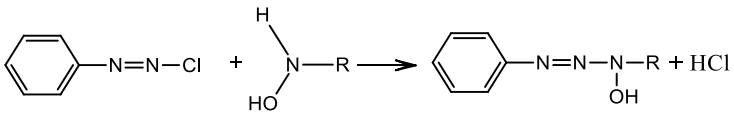
The reaction scheme shown as below.



- **Second Method**

The second method is modified version of first method, which is establised by Bamberger et al., Bamberger and Renault and Bamberger and Tschirner. The method involved a sequence of

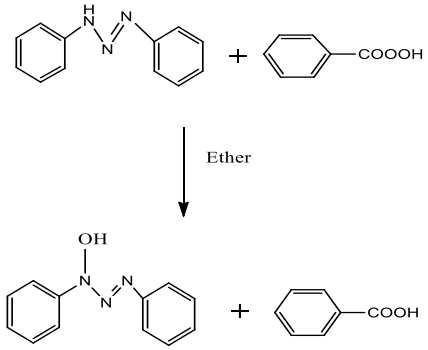
- Reduction of alkyl or aryl nitrobenzeneor substituted nitrobenzene to hydroxyl amine.
- Diazotization of aryl amine to diazonium salt
- Coupling of the aryl hydroxylamine with the diazonium salt in the acetate buffer medium of 5-6 pH at the temperature between 0-5^{o}C. The reaction is shown below:



Here, R = alkyl or aryl group.

- **Third Method**

This method was developed by Mitsuhasi and Simamura. This synthesis basically involves the oxidation of diazoaminobenzene with peroxybenzoicacid under suitable condition. The reaction can be described as follows:



Stepwise Description of Synthesis of DHA

Synthesis of Ammelines associated with category A.

A general procedure of synthesis was adopted for the preparation of Ammelines, in this section total six hydroxytriazenes were prepared which is associated with category A.

Following three steps are involved

- **Step (a): Reduction of nitro compound to hydroxylamine**

  Reagents

  - **Organic reagent (A.R.Grade)**

In present research work some aliphatic and aromatic nitro compounds have been used for the reduction purpose. Following reagents were used.

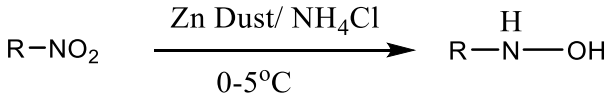
Aliphatic Nitro Compound	Aromatic Nitro Compound
Nitromethane	Meta-nitrotoluene
Nitroethane	Para-nitrotoluene
1-Nitropropane	2-bromo 4-nitrotoluene

  - **Ammonium chloride**
  - **Zinc dust**
  - **Distilled water**
  - **Rectified spirit**

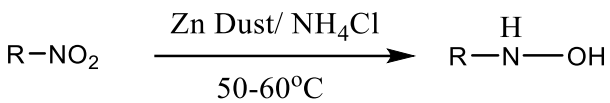
Procedure

In first step, 0.05 mole nitrobenzene or substituted nitrobenzene and 35mL of rectified spirit were taken in 500 ml beaker, and stirred mechanically. On the other hand, saturated solution of 3gm ammonium chloride was prepared in 25 ml of water. After that,NH_4Cl solution was added into nitrobenzene solution slowly and heated up to 40^oC.Then, small amount of 10 gm of zinc dust was frequently added with continuous stirring until the Zn dust was completed and maintain the temperature between 50 to 60^oC.The resulting mixture was then further stirred for next 15 minutes at 60^oC to eliminate the remaining solvent, where's if the taken nitro compound is aliphatic then temperature range should be 0-5^oC.

Reduction of aliphatic nitro compound



Reduction of aromatic nitro compound



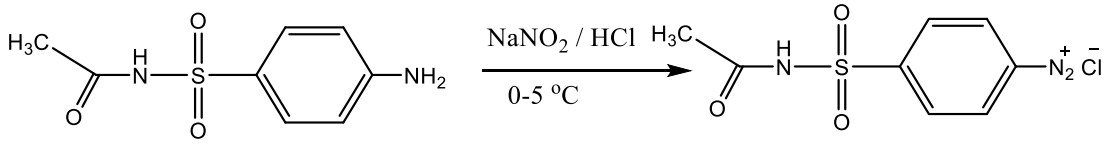
- **Step (b): Diazotization of sulfacetamide to diazonium salt**

  Reagents

  - **N-[(4-aminophenyl)sulfonyl]acetamide**
  - **Conc. HCl**
  - **Distilled water**
  - **Sodium nitrite**

Procedure

In 250 ml beaker,0.03 mol of N-[(4-aminophenyl)sulfonyl]acetamide, 15 mlconcentrated hydrochloric acid and 30 mL distilled water were used to make a reaction mixture, after that reaction mixture was kept in an ice bath for the stirring in 0-5^{o}C temperature range. In another beaker, saturated solution of 2.07 gm of sodium nitrite in water was prepared and it was also kept on an ice bath to cool. Sodium nitrite solution was added drop wise to the N-[(4-aminophenyl)sulfonyl]acetamide solution with constant stirring by a magnetic stirrer. The obtained mixture of N-[(4-aminophenyl)sulfonyl] acetamidediazonium chloride was directly used for coupling.



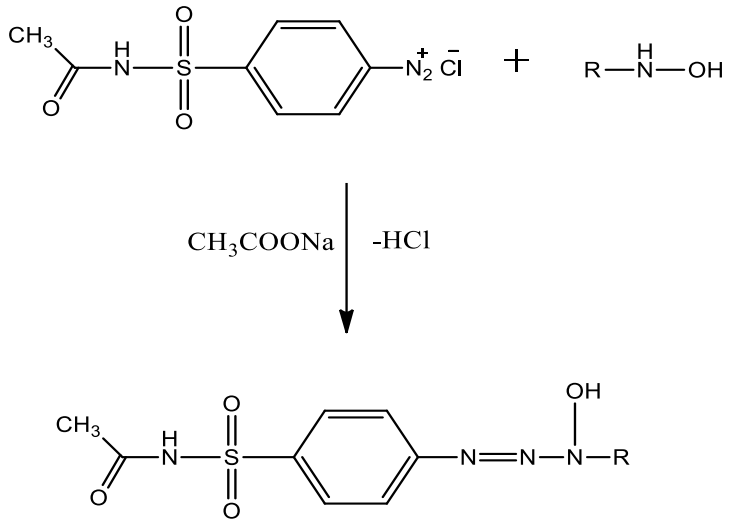
- **Step (c): Coupling**

  Reagents

  - Hydroxylamine solution obtained from step (a)
  - N-[(4-aminophenyl)sulfonyl] acetamidediazonium chloride salt obtained from step (b)
  - Sodium acetate solution

Procedure

Phenyl or substituted phenyl hydroxylamine solution [obtained from step (a)] was kept in an ice bath to maintain temperature below 5^{o}C. To this solution, diazonium salt of N-[(4-aminophenyl)sulfonyl]acetamide [obtained from step (b)] was added drop by drop. A 10% solution of sodium acetate was used for maintain the pH in between 5 to 6 into the reaction mixture, when required. When the addition of diazonium salt was completed, the mixture was stirred again for fifteen minutes. The products of coupling was washed firstly and then recrystallized using appropriate solvent. Crystals and powder form of hydroxytriazenes were obtained. The main part of this process is that phenyl hydroxyl amine was taken in excess to reduce the trouble of decomposition of product due to unreacted diazonium salt.



Characterization of DHA

All the synthesized Ammelines were characterized by following spectroscopic techniques:

- IR spectroscopic characterization
- NMR spectroscopic characterization
- Mass spectroscopic characterization

Table 1: Details of Spectral analysis of DHA -1

Ammelines-1							
IR Analysis in cm^{-1}	ν_{O-H}	ν_{N-H}	$\nu_{C=O}$	$\nu_{N=O}$	$\nu_{N=N}$	$\nu_{C=N}$	$\nu_{S=O}$
	3299	3196	1716	1590	1421	1330	1150
^{1}H NMR Analysis	**Positions of signal**		**No. of proton**	**Chemical shift (ppm)**		**Splitting**	
	1		3 H	δ 2.51		s	
	17		3 H	δ 1.92		s	
	15		1 H	δ 11.96		s	
	8		1 H	δ 12.37		s	
	3,4,5,7,10,11,13,14		8 H	δ 7.94-7.39		m	
^{13}C NMR Analysis	**Positions of signal**		**Chemical shift (ppm)**			**No. of carbon**	
	17		δ 20.87			1 C	
	1		δ 23.17			1 C	
	10,14		δ 114.55			2 C	
	7		δ 117.22			1 C	
	5		δ 120.29			1 C	
	4		δ 129.08			1 C	
	11,13		δ 129.40			2 C	
	3		δ 131.00			1 C	
	12		δ 131.85			1 C	
	2		δ 139.12			1 C	
	9		δ 142.95			1 C	

	6	δ 144.75	1 C
	16	δ 168.64	1 C
Mass Analysis	**m/z Value**		
	Calculated Value	**Experimental Value**	
	348.37	349.37	

Table 2: Details of spectral analysis of DHA -2

DHA -2							
IR Analysis in cm^{-1}	ν_{O-H}	ν_{N-H}	$\nu_{C=O}$	$\nu_{N=O}$	$\nu_{N=N}$	$\nu_{C=N}$	$\nu_{S=O}$
	3202	3065	1697	1587	1437	1337	1146
^{1}H NMR Analysis	**Positions of signal**		**No. of proton**	**Chemical shift (ppm)**		**Splitting**	
	17		3 H	δ 1.91		s	
	1		3 H	δ 2.39		s	
	15		1 H	δ 12.60		s	
	8		1 H	δ 12.32		s	
	4,6,3,7,11,13,10,14		8 H	δ 8.009-7.37		m	
^{13}C NMR Analysis	**Positions of Signal**		**Chemical Shift (ppm)**			**No. of Carbon**	
	17		δ20.66			1C	
	1		δ 23.26			1C	
	10,14		δ 120.9			2C	
	4,6		δ 119.83			2C	
	11,13		δ 129.37			2C	
	3,7		δ 129.65			2C	
	12		δ 131.95			1C	
	2		δ 140.29			1C	
	9		δ 140.77			1C	
	5		δ 144.71			1C	
	16		δ 168.79			1C	
Mass Analysis	**m/z Value**						
	Calculated Value			**Experimental Value**			
	348.37			349.37			

Table 3: Details of Spectral analysis of DHA -3

DHA -3							
IR Analysis in cm^{-1}	ν_{O-H}	ν_{N-H}	$\nu_{C=O}$	$\nu_{N=O}$	$\nu_{N=N}$	$\nu_{C=N}$	$\nu_{S=O}$
	3188	3091	1700	1590	1438	1333	1144
^{1}H NMR Analysis	**Positions of signal**		**No. of proton**	**Chemical shift (ppm)**		**Splitting**	
	1		3H	δ2.50-2.52		s	
	11		3H	δ1.93		s	
	2		1H	δ11.99		s	
	5,7, 4,8		4H	δ7.88-7.581		m	
	9		1H	δ12.03		s	
	Positions of Signal		**Chemical Shift (ppm)**			**No. of Carbon**	
	11		δ23.19			1C	
	1		δ50.85			1C	
	4,8		δ113.47			2C	

^{13}C NMR Analysis	6	δ129.42	1C
	5,7	δ130.82	2C
	3	δ145.12	1C
	10	δ168.73	1C
Mass Analysis	**m/z Value**		
	Calculated Value	**Experimental Value**	
	272.28	273.28	

Table 4: Details of spectral analysis of DHA -4

DHA -4							
IR Analysis in cm^{-1}	**ν_{O-H}**	**ν_{N-H}**	**$\nu_{C=O}$**	**$\nu_{N=O}$**	**$\nu_{N=N}$**	**$\nu_{C=N}$**	**$\nu_{S=O}$**
	3596	3191	1697	1591	1434	1337	1145
^{1}H NMR Analysis	**Positions of signal**		**No. of proton**	**Chemical shift (ppm)**		**Splitting**	
	1		3H	δ1.86		s	
	12		3H	δ2.43		s	
	2		2H	δ3.27		s	
	10		1H	δ13.17		s	
	5,6,8,9		4H	δ7.88-7.58		m	
	3		1H	δ11.99		s	
^{13}C NMR Analysis	**No. of carbon**		**Chemical shift (ppm)**			**Positions of signal**	
	1C		δ168.3			11	
	1C		δ23.19			12	
	1C		δ12.56			1	
	1C		δ59.13			2	
	2C		δ114.71			9,5	
	1C		δ129.27			7	
	2C		δ130.41			6,8	
	1C		δ145.58			4	
Mass Analysis	**m/z Value**						
	Calculated Value			**Experimental Value**			
	286.30			287.30			

Conclusion

A number of Ammelines and their substituents have been used as spectrophotometric reagents. These are the group of chelating agents which shows analytical application for detection and determination of metals. These compounds are also showed medicinal application and selected for bio-base activities such as the antimicrobial, anti-inflammatory, analgesic, insecticidal, skin healing, antidyslipidemic, antioxidant and antidiabetic activity.

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