Syntheses of di-Schiff's bases: A comparative study using benzene and water (concept of green chemistry) as solvents

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Abstract

Di-Schiff's bases are normally synthesized from aldehyde and diamine using organic solvents under conditions that remove water azeotropically. Here is a report for the preparation of di-Schiff's base using both the conventional method and pure water without a catalyst and results were compared. It was observed that yields are better and reaction time is comparatively less when water is used as a solvent.

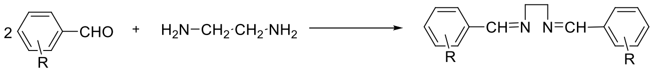
Keywords: Benzene, Water, Green chemistry.

Introduction

Di-Schiff's bases are used in organic synthesis and metal ion complexation.[1,2] These are reported to have great use as analytical, medicinal, polymer and liquid crystalline materials. Aliphatic and aromatic aldehydes condense with aliphatic diamine to give N, N'-substituted di-Schiff's base. The preparation of di-Schiff's base has been carried out by refluxing the mixture of aliphatic diamine and aromatic aldehyde in organic solvents like toluene and benzene in Dean-Stark apparatus under azeotropic condition in order to separate the water formed.[3,4] The use of solvents is a constant source of worry since it gives rise to toxicity, environmental hazard, pollution and waste treatment issues. Moreover, solvents generally account for the major source of the wasted mass of a given process or a synthetic pathway. From a strictly Green Chemistry point of view, the best answer to this problem would be to run the reactions under neat conditions. The concept of Green Chemistry has been defined as the design of chemical products and processes to reduce or eliminate the use and generation of hazardous substances. Consequently, many efforts have been devoted to the finding of sustainable reaction media, and notably the use of water as solvent has attracted much interest in recent years. Indeed, water offers many advantages because it is a cheap, readily available, non-toxic and non-flammable solvent, thus being very attractive from both an economical and an environmental point of view.[5]The solvents that currently remain the basis of our chemical operations are still largely organic and contain various health and environmental concerns. Discovering the new applications for ancient solvent systems such as water will continue to be an important area of investigation for Green Chemistry researchers. There are major opportunities to extend the use of water as a solvent for organic reactions.[6] In recent years environmentally benign synthetic methods have received considerable attention and some solvent free protocols like water based reaction, microwave irradiation and grindstone method were developed.[7] Previously, synthesis of di-Schiff's bases was reported from our laboratory using benzene as the solvent. These compounds were used as intermediates for the formation of tetrahydroimidazoles.[8-10] Here we are reporting the synthesis of few di-Schiff's bases by two methods i.e. using benzene as solvent in Dean-Stark apparatus as well as water and comparing the results. It was found that di-Schiff's base can be synthesized in better yield in pure water compared to that in organic solvent i.e. benzene with much reduced reaction time. Few compounds reported here are already reported by us using benzene as solvent (compound no. 1a, 1b, 1c, 1e, 1f, 1g). M.P. of the compounds synthesized by the two different methods were found to be nearly same therefore are being reported as common.

Results and Discussion

The compounds were synthesized as per the following scheme-



1(a-h)

Scheme used for the preparation of di-Schiff's bases (1a-h)

In method 1, dry benzene was used as the solvent. Appropriate aldehyde (double the mole of ethylenediamine) and ethylenediamine were refluxed together in dry benzene under Dean Stark assembly to remove the water azeotropically using molecular sieves of A4 size. Reaction mixture was then processed as per the detail given below. In method 2, aldehyde and ethylenediamine were taken in water and stirred at room temperature without using any drying agent or catalyst. Results for the reaction between various aldehydes and ethylenediamine are given in the table 1. It was found that method 1 gave compounds with % yield in the range of 60-92% and reaction time was 8h. While when water was used as the solvent, % yield was from 80-95% and reaction time was 1-3h.

Table 1: Data of the synthesized compounds

1(a-h)	R	Reaction time (h)		Yield (%)		M.P. (°C)
		Water	Benzene	Water	Benzene	
a	4-CH_3O	2	8	85	82	103-106
b	H	3	8	83	80	58-62
c	4-Cl	1	8	80	60	130-132
d	4-F	2.5	8	84	72	135-137
e	4-$(CH_3)_2N$	2	8	84	81	170-174
f	3,4-OCH_3	2	8	80	76	150-153
g	4-OH	1	8	95	92	90-92
h	*(using cinnamaldehyde $C_6H_5CH = CHCHO$)	3	8	88	63	116-120

*compound formed is N1, N2-bis (3-phenylallylidene) ethane-1, 2-diamine

Materials and Methods

The chemicals and solvents used for the experimental work were commercially procured from different chemical suppliers, such as E. Merck India Ltd. Mumbai (India), S.D. Fine-Chem Ltd. Mumbai (India), CDH Mumbai (India), and Qualigens, Mumbai (India). The solvents and reagents were of laboratory reagent grade. All the synthesized compounds were dried in vacuum desiccators over silica gel. The melting point (M.P.) of each compound was determined using open capillary tubes in the HICON digital instrument (India). Completion of the reaction was monitored using thin-layer chromatography (TLC). The spots were visualized either by exposing the developed and dried plates to iodine vapors or in the ultraviolet (UV) chamber. The 1H NMR spectra of the compounds were recorded on the Bruker DPX-300 NMR spectrometer (Germany) at 300 MHz, using $CDCl_3$ as solvent. Tetramethylsilane was used as an internal standard, and the values of the chemical shift were given in the δ scale.

Preparation of (1a) is representative of the general procedure employed in two methods.

Method 1

Preparation using organic solvent (benzene)

Anisaldehyde (3 mmol, 0.4 g) and ethylenediamine (1.5 mmol, 0.09 g) were taken in dry benzene (25 mL) and refluxed under Dean-Stark assembly in order to remove the water azeotropically. Molecular sieves of 4A size were also added. After removal of water the mixture was refluxed for another 8 h. Excess benzene was distilled off and the solid mass so obtained was recrystallized using methanol.

Method 2

Preparation using water

Anisaldehyde (3 mmol, 0.4 g) was taken in water (30mL) and ethylenediamine (1.5 mmol, 0.09 g) was added to the mixture. The reaction mixture was continuously stirred on magnetic stirrer at room temperature (time mentioned in the table). The solid thus obtained was filtered off and washed with cold water and dried under vacuum. The solid was recrystallized form mixture of dichloromethane and petroleum ether.

N 1, N2-bis (4-methoxybenzylidene) ethane-1, 2-diamine 1a. (0.32 g, 85%): white prism, mp 103-106°C

1H NMR: 8.2(2H, s, 2×CH=N), 7.62-7.64(4H, d, 2, 6, 2', 6 Ar-H), 6.88-6.9(4H, d, 3, 5, 3', 5'Ar-H), 3.91(4H, s, 2×CH_2), 3.8(6H, s, 2×OCH_3).

N1, N2-bis (dibenzylidene) ethane-1, 2-diamine 1b. (0.26 g, 83%): very light yellow prism, mp 58-62°C

1H NMR: 8.27(2H, s, 2×CH=N), 7.70-7.69(4H, d, 2, 6, 2', 6 Ar-H), 7.38-7.36(4H, d, 3, 5, 3', 5' Ar-H), 3.9(4H, s, 2×CH_2)

N1, N2-bis (4-chlorobenzylidene) ethane-1, 2-diamine 1c. (0.33 g, 80%): white crystals, 130-132°C

1H NMR: 8.21(2H, s, 2×CH=N), 7.61-7.59(4H, d, 2, 6, 2', 6' Ar-H), 7.34-7.32(4H, d, 3, 5, 3', 5' Ar-H), 3.93(4H, s, 2×CH_2).

N1, N2- bis (4-fluorobenzylidene) ethane-1, 2-diamine 1d. (0.35 g, 84%): very light yellow prism, mp 135-137°C

1H NMR: 8.65(2H, s, 2×CH=N), 7.81 (4H, d, 3, 5, 3', 5' Ar-H), 7.36 (4H, d, 2, 6, 2', 6' Ar-H), 3.95 (4H, s, 2×CH_2).

N1, N2-bis (4-dimethylaminobenzylidene) ethane-1, 2-diamine 1e. (0.33 g, 84%): light yellow prism, mp 170-174°C

1H NMR: 8.14 (2H, s, 2×CH=N), 7.57-7.55 (4H, d, 2, 6, 2', 6', Ar-H), 6.66-6.64 (4H, d, 3, 5, 3', 5' Ar-H), 3.86 (4H, s, 2×CH_2), 2.97 (12H, s, 2×N $(CH_3)_2$).

N1, N2-bis (3, 4-dimethoxybenzylidene) ethane-1,2-diamine 1f. (0.36 g, 80%): light yellow prisms, 150-153°C

1H NMR: 8.17(2H, s, 2×CH=N), 7.24(2H, d, 2, 2' Ar-H), 7.10-7.07(2H, d, 6, 6' Ar-H), 3.90-3.88(16H, s, 4×OCH_3, 2×CH_2).

N1, N2- bis (4-hydroxybenzylidene) ethane-1, 2-diamine 1g. (0.27 g, 95%): greenish yellow prisms, mp 90-92 °C

1H NMR: 8.3(2H, s, 2×CH=N), 6.7-7.4(8H, m Ar-H), 3.9(4H, s, 2×CH_2).

N1, N2-bis (3-phenylallylidene) ethane-1, 2-diamine 1h. (0.42 g, 88%): yellow plates, mp 116-120 °C

1H NMR: 8.05(2H, d, 2×CH=N), 7.45(2H, d, 2×CH=CH), 7.26-7.37(8H, m, Ar-H), 6.87-6.97(2H, m, 2×CH=CH), 3.85(4H, s, 2×CH_2).

Conclusion

We have synthesized di-Schiff's bases by using different solvents. Di-Schiff's base formation using water required less time compared to the time consumed by the synthesis in organic solvent (dry benzene). The percentage yield was also high in the aqueous method compared to the synthesis in organic solvent. The method 2, i.e. using water is convenient, easy to use, did not require any drying agent or catalyst, fast and gives better yield.

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Conflict of Interest

None.

References

1. Van den Ancker TR, Cave GW, Raston CL. Benign approaches for the synthesis of bis-imine Schiff bases. *Green Chem.* 2006;8(1):50-3.
2. Correa WH, Scott JL. Synthesis and characterisation of macrocyclic diamino chiral crown ethers. *Molecules.* 2004;9(6):513-9.
3. Sharma V. Synthesis of Novel Architectures from Triazinyl Hydrazines and Various Carbonyl Compounds; 2020.
4. Tanaka K, Shiraishi R. Clean and efficient condensation reactions of aldehydes and amines in a water suspension medium. *Green Chem.* 2000;2(6):272-3.
5. Simon MO, Li CJ. Green chemistry oriented organic synthesis in water. *Chem Soc Rev.* 2012;41(4):1415-27.
6. Horvath IT, Paul T. Anastas. Innovations and green chemistry. *Chem Rev.* 2007;107(6):2169-73.
7. Varma RS, Dahiya R, Kumar S. Clay catalyzed synthesis of imines and enamines under solvent-free conditions using microwave irradiation. *Tetrahedron Lett.* 1997;38(12):2039-42.
8. Khan MSY, Chawla G. Tetrahydroimidazoles-A promising group of expected NSAIDS-their synthesis and anti-inflammatory activity. *Indian J Chem.* 2002;41B:653-63.
9. Sharma V, Khan MS. Synthesis of novel tetrahydroimidazole derivatives and studies for their biological properties. *Eur J Med Chem.* 2001;36(7-8):651-8.
10. Kumar U, Bawa S, Ranjan C, Chawla G. Design, syntheses, characterization, and evaluation of 2-substituted-1, 3-bis (1-naphthylmethyl)-imidazolidine derivatives in search of safer nonsteroidal anti-inflammatory drugs. *Drug Dev Ther.* 2015;6(2).

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