International Journal of Advance and Applied Research
www.ijaar.co.in
ISSN – 2347-7075 Impact Factor – 8.141
Peer Reviewed Bi-Monthly
Vol. 6 No. 18 March - April - 2025

Application of Acidic [BTEAC][OX.2H2O] Deep Eutectic Solvent/Catalyst; Green Solvent for Synthesis of Hydrazone Schiff Bases From 2-acetyl-1-naphthol

Suchita B. Wankhede
Department of Chemistry, Amolakchand Mahavidyalaya, Yavatmal (MS) India
Corresponding Author – Suchita B. Wankhede
DOI - 10.5281/zenodo.15259328

Abstract:

Considering enormous applications of hydrazone schiff bases in various fields, a series of 1-(1-hydroxynaphthalen-2-yl)ethanone-substituted-benzoylhydrazone (H_2L^{1}-H_2L^4) schiff bases were synthesized using green, environmentally benign acidic benzyltriethylammoniumchloride [BTEAC] deep eutectic solvents. From the study of optimized reaction conditions, [BTEAC][oxalic acid.2H_2O] DES gives excellent reaction yield within reduced time. Catalytic property of DES was further compared with conventional reflux method; obviously [BTEAC][oxalic acid.2H_2O] DES proves to be good solvent as well as catalyst along with possessing recoverable and reuse capability.

Keywords: Green Solvent, Deep Eutectic Solvent, Hydrazone Schiff Bases, Environment Benign Method.

Introduction:

Acyl hydrazones are special type of Schiff bases, possessing interlinked nitrogen atoms attached to carbonyl group (R_1R_2C=NNHCOR_3). Introducing a >C=O group into the hydrazide portion enhances the electron delocalization of the hydrazone, which is an attractive functional group in synthesis of coordination complexes [1] and also in heterocyclic synthesis [2]. Presence of hydrazone functional group and incorporation of various biologically active groups increases biological activity in hydrazone schiff bases. Several derivatives of hydrazone schiff bases reported in literature exhibits promising antiviral, anti-fungal, antibacterial, anti-tubercular, anti-inflammatory, anti-oxidant etc [3]. Hydrazone Schiff bases are conventionally synthesized in organic solvents such as ethanol, methanol, dimethyl sulfoxide, dimethylformamide, etc., using catalysts like acetic acid, concentrated hydrochloric acid, concentrated sulfuric acid, etc. [4]. However, challenges such as excessive solvent and catalyst usage, long reaction times, high temperatures, and low yields persist in conventional synthesis [5]. Additionally, organic solvents pose toxicity issues, and catalysts are difficult to reuse and recover. Therefore, a new set of green condition is necessary to mitigate these drawbacks of the conventional approach.

In search of green and environmentally benign procedures 'Deep eutectic solvents '(DES), a green and new generation solvent satisfy both catalyst as well as solvent properties in numerous organic transformations [6]. It was first introduced by Abbott's group in 2003 [7], represent a new class of nonaqueous solvents with properties similar to ionic liquids (ILs). Aim of present work is compare conventional method of synthesis of hydrazone schiff bases from our previous work [8-10] using acidic BTEAC, DESs as greener solvent under optimized condition. *[BTEAC][oxalic acid.2H_2O]* DES, proves to be a remarkable potential solvent/catalyst to increase yield of product within short time.

Experimental:

Material and Methods:

Starting materials are synthesized from analytical grade (AR) chemicals and solvents. They are used without purification and procured from S. D. Fine. Synthesis of all hydrazone schiff bases were monitored by thin layer chromatography (TLC) pre-coated silica gel plates and visualising using UV chamber. Melting points were determined by the open capillary method, using electrical melting point apparatus. The IR spectra were recorded in KBr disc in the range of 4000-350 cm^{-1}. ^{1}H-NMR are recorded in DMSO-d^6 solvent on Bruker 400MH_z spectrophotometer, using TMS as internal standard. 2-acetyl-1-naphthol [11] and substituted benzohydrazides are synthesized from literature methods [12].

Preparation of deep eutectic solvents (DESs):

Acidic BTEAC, DESs were synthesized by method given in literature [13]. Benzyltriethylammoniumchloride *[BTEAC]* (1 mmol) and acid (1 mmol) were added into a round bottom flask. The mixture was heated at 100 °C and stirred for 15 min for malonic acid and 1 h for oxalic, citric acid and benzoic acids, until a clear, colourless liquid was obtained.

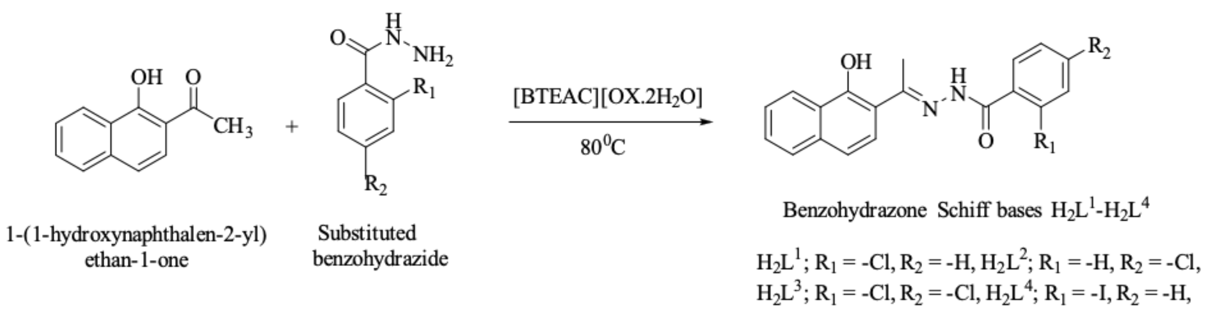
General procedure for the synthesis of 1-(1-hydroxynaphthalen-2-yl)ethanone-substituted benzoylhydrazone (H_2L^1, H_2L^2, H_2L^3 & H_2L^4):

Conventional method:

To a hot ethanolic solution (15ml) of substituted benzoylhydrazide (0.01mol), hot ethanolic solution (15ml) of 2-acetyl-1-naphthol (0.01mol) was added with continuous stirring in round bottom flask and reaction mixture was heated under reflux on water bath for 3-4 hr. After cooling, the coloured solid obtained was filtered off, washed with ethanol and dried under vaccume of $CaCl_2$. It was finally recrystallized from DMF- ethanol mixture (1:4 v/v).

Using DES:

A mixture of benzoyl hydrazines (0.1 mmol) and 2-acetyl-1-naphthol (0.1 mmol) and 1.5 ml DES was stirred at optimized temperature 80 ºC for an appropriate time (Scheme 1). The reaction was monitored by TLC (ethylacetate:hexane). After completion of reaction, the mixture was diluted to water, filtered and dried to get product and recrystallized from 1:1 (v/v) DMF/ethanol. The DES could be recovered by vaporization of its aqueous solution under vacuum to furnish the used DES for the next reaction run.



Scheme 1. Synthesis of benzohydrazone schiff bases in *[BTEAC][oxalic acid.2H_2O]* DES

Table 1. Analytical data of Schiff bases H_2L^1 - H_2L^4

Hydrazone Schiff base	Molecular Formula	Molecular Weight	Colour	Melting point	Elemental Analysis found (calculated)			
					C%	H%	N%	Cl%
H_2L^1	$C_{19}H_{15}ClN_2O_2$	338.79	Lemon Yellow	211	67.28 (67.36)	4.18 (4.46)	7.98 (8.27)	10.49 (10.46)
H_2L^2	$C_{19}H_{15}ClN_2O_2$	338.79	Golden Yellow	202	67.01 (67.36)	3.88 (4.46)	8.08 (8.27)	10.00 (10.46)
H_2L^3	$C_{19}H_{14}Cl_2N_2O_2$	373.23	Yellow	170	61.16 (61.14)	3.42 (3.78)	7.21 (7.51)	18.43 (19.00)
H_2L^4	$C_{19}H_{15}IN_2O_2$	430.24	Pale Yellow	173	52.78 (53.04)	3.04 (3.51)	6.31 (6.51)	—

1-(1-hydroxynaphthalen-2-yl)ethanone-2-chlorobenzoylhydrazone (H_2L^1) :

FT-IR (KBr, 4000–400 cm^{1}): υ(N-H) 3190, υ(O-H) 2995, υ(C=O) 1637, υ(C=N) 1589 [14].

^{1}H-NMR (400MH$_z$,DMSO-d$_6$): δ 14.74, (1H, S, phenolic OH); δ 11.62, (1H, S, imino NH); δ 2.52, (3H, S, methyl); δ 8.29, (1H, d, naphthyl); δ 7.79, (1H, d, phenyl); δ 7.45-7.62 ppm, (5H, m, naphthyl); δ 7.25-7.50 ppm, (3H, m, phenyl) [15].

1-(1-hydroxynaphthalen-2-yl)ethanone-4-chlorobenzoylhydrazone (H_2L^2):

FT-IR (KBr, 4000–400 cm^{1}): υ(N-H) 3211, υ(O-H) 3005, υ(C=O) 1633, υ(C=N) 1593.

^{1}H-NMR (400MH$_z$,DMSO-d$_6$):δ 14.82, (1H, S, phenolic OH); δ 11.34, (1H, S, imino NH); δ 2.55, (3H, S, methyl); δ 8.28, (1H, d, naphthyl); δ 7.40-7.85 ppm, (5H, m, naphthyl); δ 7.54-7.99 ppm, (4H, m, phenyl)

1-(1-hydroxynaphthalen-2-yl)ethanone-2,4-chlorobenzoylhydrazone (H_2L^3):

FT-IR (KBr, 4000–400 cm^{1}): υ(N-H) 3207, υ(O-H) 2995, υ(C=O) 1629, υ(C=N) 1587.

^{1}H-NMR (400MH$_z$,DMSO-d$_6$): δ 14.75, (1H, S, phenolic OH); δ 11.73, (1H, S, imino NH); δ 2.51, (3H, S, methyl); δ 8.36, (1H, d, naphthyl); δ 7.81, (1H, d, phenyl); δ 7.66, (1H, S, phenyl); δ 7.58-7.72, (5H, m, naphthyl)

1-(1-hydroxynaphthalen-2-yl)ethanone-2-iodobenzoylhydrazone (H_2L^4):

FT-IR (KBr, 4000–400 cm^{1}): υ(N-H) 3194, υ(O-H) 2997, υ(C=O) 1654, υ(C=N) 1583.

^{1}H-NMR (400MH$_z$,DMSO-d$_6$): δ 14.85, (1H, S, phenolic OH); δ 11.68, (1H, S, imino NH); δ 2.51, (3H, S, methyl); δ 8.36, (1H, d, naphthyl); δ 7.98, (1H, d, naphthyl); δ 7.88-7.89, (2H, dd, phenyl); δ 7.72 (1H, d, naphthyl); δ 7.15-7.30, (4H, m, aromatic)

Results and Discussion:

We begin our study with synthesis of 1-(1-hydroxynaphthalen-2-yl)ethanone-2-chlorobenzoylhydrazone (**H_2L^1**); prepared form 2-acetyl-1-naphthol and 2-chlorobenzoydrazide as model reaction in *[BTEAC][oxalic acid.2H_2O]* DES as solvent as well as catalyst. To explore and optimise reaction conditions, various catalyst mol% of [BTEAC][oxalic acid.2H_2O] DES at different temperature was studied (table 2, entry 1-7). As shown in Table 2, desired product was obtained with good yield (92%) using 20 mol% of *[BTEAC][oxalic acid.2H_2O]* DES at 80ºC within least time (table 2, entry 7). Result shows that, higher the reaction temperature, more efficiently reaction could proceed in short time. Now same reaction condition was applied using *[BTEAC][malonic acid]*, *[BTEAC][citric acid]* and *[BTEAC][Benzoic acid]* DESs, under optimum temperature; 80ºC. Results reveals that *[BTEAC][oxalic acid.2H_2O]* DES was played better role as catalyst as well as solvent than others (table 2, entry 8-10).

Table 2. Effect of reaction time, temperature and catalyst mol% and yield on synthesis of 1-(1-hydroxynaphthalen-2-yl)ethanone-2-chlorobenzoylhydrazone (H_2L^1)

Entry	DES/Solvent	Catalyst mol%	Temp.(° C)	Time (min)	Yield
1	*[BTEAC][oxalic acid.2H_2O]*	5	70	50	50
2	*[BTEAC][oxalic acid.2H_2O]*	5	75	42	65
3	*[BTEAC][oxalic acid.2H_2O]*	5	80	25	78
4	*[BTEAC][oxalic acid.2H_2O]*	5	85	22	76
5	*[BTEAC][oxalic acid.2H_2O]*	10	80	20	82
6	*[BTEAC][oxalic acid.2H_2O]*	15	80	18	88
7	***[BTEAC][oxalic acid.2H_2O]***	**20**	**80**	**10**	**92**
8	*[BTEAC][malonic acid]*	20	80	25	80
9	*[BTEAC][citric acid]*	20	80	40	72
10	*[BTEAC][Benzoic acid]*	20	80	45	68
11	Ethanol/CH_3COOH	-	70-80	240	65
12	Methanol/CH_3COOH	-	70-80	245	60

Model reaction was then compared with conventional reaction conditions (table 2, entry 11-12). The conventional method showed that synthesis of schiff bases also delivered the expected product but with poor yield and these reports still suffered intrinsic drawbacks such as the requirement of long reaction time and volatile organic solvent. All synthesized schiff bases are stable to room temperature, non-hygroscopic and insoluble in water (table 1). IR and ^{1}H-NMR data matches with the structure of hydrazone schiff bases.

Table 3. Comparison of % yield and time of hydrazone Schiff's bases (H_2L^1 - H_2L^4) in conventional and *[BTEAC][oxalic acid.2H_2O]* DES

Hydrazone schiff bases	R_1	R_2	Conventional solvent Ethanol(CH_3COOH) %yield (time)	*[BTEAC][oxalic acid.2H_2O]* DES %yield (time)
H_2L^1	-Cl	-H	65 (240 min)	90 (10 min)
H_2L^2	-H	-Cl	60 (200 min)	92 (10 min)
H_2L^3	-Cl	-Cl	68 (260 min)	85 (15 min)
H_2L^4	-I	-H	62 (300 min)	82 (18 min)

Applicability of *[BTEAC][oxalic acid.2H$_2$O] DES* was further investigated for synthesis of H_2L^2 - H_2L^4 hydrazone schiff bases and also compared with conventional method. All schiff bases are obtained in good isolated yield than in conventional solvent within minimum time (table 3, entry 1-4). We have also studied recyclability of DES 1 under the optimized conditions. After completion of the reaction, the reaction mixture was poured in ice cold water and the product was filtered. The *[BTEAC][oxalic acid.2H$_2$O]* was recovered by simply evaporating water from the reaction mass after filtration of the solid product. The Deep Eutectic Solvent recovered from the previous run was reused for the next reaction without further purification [16]. This procedure was repeated several times, and the catalytic activity of DES was slightly changed after 4th cycle.

Conclusion:

The current work was featured by outstanding performance of *[BTEAC][oxalic acid.2H$_2$O]* DES in synthesis of hydrazone schiff bases. The reaction was compared with conventional method using ethanol, gives excellent yield within short time. Simple method of preparation of DES, high stability, remarkable potential to act as solvent as well as catalyst and easy recover ability, creates a new hope in organic transformations to replace dangerous volatile solvents.

References:

1. Fallah-Mehrjardi, M., Kargar, H., & Munawar, K. S. (2023). Tridentate ONO hydrazone Schiff base complexes in organic transformations: Catalytic and mechanistic studies. *Inorganica Chimica Acta*, *560*, 121835. https://doi.org/10.1016/j.ica.2023.121835
2. Channabasappa, V., Kumara, K., & Kariyappa, A. K. (2021). Design, synthesis of coumarin tethered 1,2,3-triazoles analogues, evaluation of their antimicrobial and α-amylase inhibition activities. *Journal of Chemical Sciences*, *133*(4). https://doi.org/10.1007/s12039-021-01997-0
3. Sharma, P., Sharma, D., Sharma, A., Saini, N., Goyal, R., Ola, M., Chawla, R., & Thakur, V. (2020). Hydrazone comprising compounds as promising anti-infective agents: chemistry and structure-property relationship. *Materials Today Chemistry*, *18*, 100349. https://doi.org/10.1016/j.mtchem.2020.100349
4. Bashir, M., Dar, A. A., & Yousuf, I. (2023). Syntheses, structural characterization, and cytotoxicity assessment of novel MN(II) and ZN(II) complexes of Aroyl-Hydrazone Schiff Base Ligand. *ACS Omega*, *8*(3), 3026–3042. https://doi.org/10.1021/acsomega.2c05927
5. Zangade, S., & Patil, P. (2020). A review on solvent-free methods in organic synthesis. *Current Organic Chemistry*, *23*(21), 2295–2318. https://doi.org/10.2174/1385272823666191016165532
6. Khandelwal, S., Tailor, Y. K., & Kumar, M. (2015). Deep eutectic solvents (DESs) as eco-friendly and sustainable solvent/catalyst systems in organic transformations. *Journal of Molecular Liquids*, *215*, 345–386. https://doi.org/10.1016/j.molliq.2015.12.015
7. Abbott, A. P., Capper, G., Davies, D. L., Rasheed, R. K., & Tambyrajah, V. (2002). Novel solvent properties of choline chloride/urea mixtures. *Chemical Communications*, *1*, 70–71. https://doi.org/10.1039/b210714g

8. Wankhede, S. B. & Patil, A. B., (2016). Synthesis, spectral characterization and thermal studies of Ti (III), Cr (III) and Mn (III) complexes derived from 2-Chlorobenzohydrazone schiff's base. *Der Pharma Chemica, 8(13)*, 22-26.
9. Wankhede, S. B., & Patil, A. B. (2018). Studies on Ti(III), Cr(III) and Fe(III) complexes with 1-(1-hydroxynaphthalen-2-yl)ethanone-4-chlorobenzoylhydrazone ligand: Synthesis, Physicochemical and Antimicrobial activity. *Journal of Pharmaceutical, Chemical and Biological Sciences*. *6(1)*, 25-33.
10. Wankhede, S. B. (2021). Oxovanadium(IV) Complexes: Synthesis, Spectral and Antimicrobial Studies Derived from Dibasic Tridentate (ONO) Donor Aroylydrazone Schiff's Bases. *International Journal of Advanced Research in Science, Communication and Technology (IJARSCT). 12(4),* 94-102. DOI: 10.48175/IJARSCT-2358
11. Nencki, M. Sieber, N., (1881). Überdies Verbindungen der ein-und Zweibasischen Fattsauren mit Phenlen, *Journal fur Praktische Chemie, 23*, 147-156.
12. Vogel A. I. (1978). A Text Book of Practical Organic Chemistry. 5th Ed. London: Longman.
13. Paveglio, G., Milani, F., Sauer, A., Roman, D., Meyer, A., & Pizzuti, L. (2020). Structure-Physical Properties Relationship of Eutectic Solvents Prepared from Benzyltriethylammonium Chloride and Carboxylic Acids. *Journal of the Brazilian Chemical Society*. https://doi.org/10.21577/0103-5053.20200208
14. Alaghaz, A. M., Zayed, M. E., Alharbi, S. A., Ammar, R. A., & Elhenawy, A. (2014). Synthesis, characterization, biological activity, molecular modeling and docking studies of complexes 4-(4-hydroxy)-3-(2-pyrazine-2-carbonyl)hydrazonomethylphenyl-diazen-yl-benzenesulfonamide with manganese(II), cobalt(II), nickel(II), zinc(II) and cadmium(II). *Journal of Molecular Structure*, *1084*, 352–367. https://doi.org/10.1016/j.molstruc.2014.12.041
15. Silverstein, R. M. Bassler, G. C. and Morrill, T.C. (1950). '*SpectroscopicIdentification of Organic Compounds*', 5th Ed. John Wiley and Sons, New York.
16. Nguyen, T., Nguyen, C. T., & Tran, P. H. (2019). Synthesis of a new series of 2-hydroxy-5-iodo-N'-(1-arylethylidene)benzohydrazides using a deep eutectic solvent as solvent/catalyst under sonication. *Heliyon*, *5*(8), e02353. https://doi.org/10.1016/j.heliyon.2019.e02353