

ORIGINAL ARTICLE

Ammonium Lauryl Sulfate: An Anionic Surfactant Catalyzed One Pot Green Synthesis of 1H-Benzo[d]imidazoles, Quinoxalines and 2,3-Dihydro-1H-benzo[b][1,4]diazepines at Room Temperature

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ABSTRACT

We have developed a greener synthetic method for the synthesis of 1H-benzo[d]imidazoles, quinoxalines and 2,3-dihydro-1H-benzo[b][1,4]diazepines from the diversity of aromatic aldehydes, 1,2-diketones and ketones respectively at room temperature using anionic surfactant, ammonium lauryl sulfate (ALS) as an efficient catalyst and water as a solvent. This protocol gave 1H-benzo[d]imidazoles, quinoxalines and 2,3-dihydro-1H-benzo[b][1,4]diazepines in good to excellent yield with high purity.

Keywords: 1H-benzo[d]imidazoles, quinoxalines, 2,3-dihydro-1H-benzo[b][1,4]diazepines, anionic surfactant, ammonium lauryl sulfate.

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INTRODUCTION

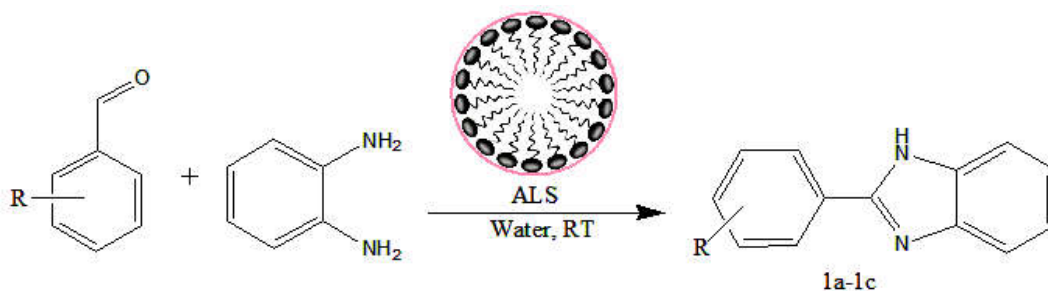
In synthetic organic chemistry, development of green methodologies in terms of solvent choice and catalyst design to reduce the waste generation is a key step in the reaction. Concept of green chemistry has open new vistas for synthetic chemists that encourage moving towards sustainable and innovative approach [1-8]. One of the important areas of green chemistry is to minimize energy consumption and replacement of toxic solvents with environmentally benign solvents. Water as a solvent has gained much attention as it is safe, inexpensive, non-toxic and environmentally friendly. Heterocycles represents significant compounds in drugs and pharmaceutically relevant substances [9]. Quinoxalines, benzodiazepines and benzimidazoles are the important class of nitrogen containing biologically active heterocyclic compounds. They are known to exhibit broad and diversified biological activities and thus, have achieved increasing interest in medicinal and pharmaceutical chemistry [10-21]. Therefore, their synthesis is desirable under the conventions of green chemistry [22]. Herein, we report a convenient and green approach for the synthesis of 1H-benzo[d]imidazoles, quinoxalines and 2,3-dihydro-1H-benzo[b][1,4]diazepines using ammonium lauryl sulfate as an efficient catalyst and water as a solvent.

MATERIALS AND METHODS

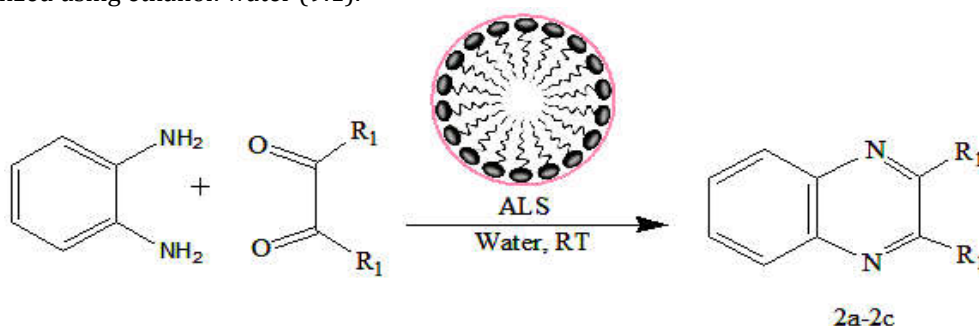
All chemicals and reagents were purchased from Hi-media and Sigma-Aldrich, and used without further purification. BRUKER AVANCE DRX-400 MHz spectrophotometer was used to record ¹H NMR spectra of synthesized compounds at ambient temperature using TMS as an internal standard.

General Procedure for the Synthesis of 1H-Benzo[d]imidazoles

To the 100 mL round bottom flask, 2 mmol aromatic aldehyde, 2 mmol benzene-1,2-diamine and 2 mol % of 30 % ALS in 2 mL distilled water were taken and stirred on magnetic stirrer at room temperature (**Scheme 1**). Reaction progress was monitored by silica gel TLC plates using hexane and ethyl acetate (70:30) solvent system. After completion of the reaction, crude solid product formed was washed with distilled water and dried. Recrystallization was done using ethanol.

Scheme 1. Synthesis of 1*H*-benzo[*d*]imidazoles**General Procedure for the Synthesis of Quinoxalines**

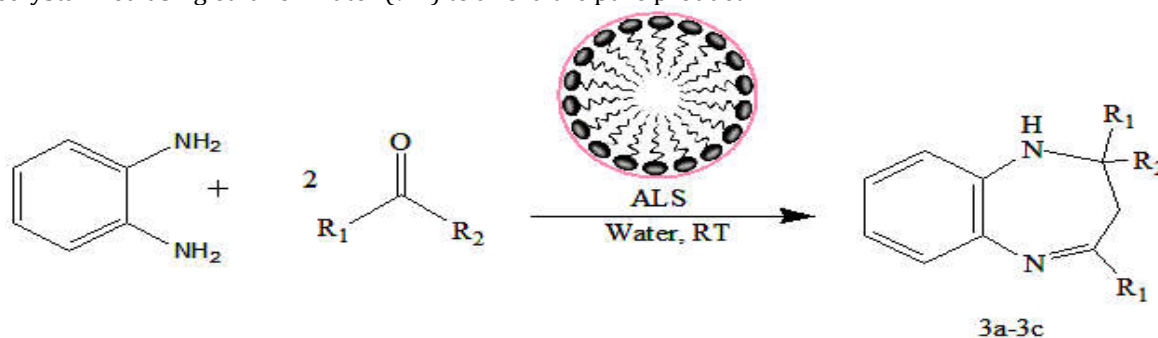
A mixture of 2 mmol benzene-1,2-diamine, 2 mmol 1,2-diketone and 2 mol % of 30 % ALS in 2 mL distilled water was taken in 100 mL round bottom flask and was stirred at room temperature (**Scheme 2**). Reaction progress was monitored by silica gel TLC plates using hexane and ethyl acetate (80:20) solvent system. After completion of the reaction, the crude solid product formed was filtered and recrystallized using ethanol: water (9:1).



Scheme 2. Synthesis of quinoxalines

General Procedure for the Synthesis of 2,3-Dihydro-1*H*-benzo[*b*][1,4]diazepines

To the 100 mL round bottom flask, a mixture of 2 mmol benzene-1,2-diamine, 4 mmol ketone and 2 mol % of 30 % ALS in 2 mL distilled water was stirred at room temperature (**Scheme 3**). Reaction progress was monitored by silica gel TLC plates using hexane and ethyl acetate (80:20) solvent system. After completion of the reaction, reaction mixture was washed with distilled water and crude product was extracted with dichloromethane. The organic extracts were dried over anhydrous Na₂SO₄ and recrystallized using ethanol: water (9:1) to afford the pure product.

Scheme 3. Synthesis of 2,3-Dihydro-1*H*-benzo[*b*][1,4]diazepines**RESULTS AND DISCUSSION**

In our present study, reaction of benzene-1,2-diamine was carried out with aromatic aldehyde, 1,2-diketone and ketones to synthesis 1*H*-benzo[*d*]imidazoles (1a-1c), quinoxalines (2a-2c) and 2,3-dihydro-1*H*-benzo[*b*][1,4]diazepines respectively using ammonium lauryl sulfate (ALS) (**Table 1**). 2 mol% of 30% ALS effectively catalyze one pot synthesis of the above compounds in good to excellent yield at room temperature and their structures are presented in figure 1. The plausible mechanism for the formation of 1*H*-benzo[*d*]imidazoles, quinoxalines and 2,3-dihydro-1*H*-benzo[*b*][1,4]diazepines is suggested in scheme 4, 5 and 6 respectively. Ammonium lauryl sulfate is an anionic surfactant that undergoes micelle

formation in water. Its hydrophobic ends surround organic substrates, thereby inducing collisions among them, which ultimately increase the rate of the reaction. Water formed during the reaction was excluded by the hydrophilic core of the micelles, leading to the formation of the product [23].

Table 1. Synthesis of 1*H*-benzo[*d*]imidazoles (1a-1c), quinoxalines (2a-2c) and 2,3-dihydro-1*H*-benzo[*b*][1,4]diazepines (3a-3c) using 2 mol% of 30% ammonium lauryl sulfate

Entry	Product	Benzaldehyde	1,2-Diketone	Ketone	Time (min)	% Yield
1	1a	<i>o</i> -ClC ₆ H ₄ CHO	-	-	45	85
2	1b	<i>o</i> -CH ₃ C ₆ H ₄ CHO	-	-	60	79
3	1c	<i>p</i> -FC ₆ H ₄ CHO	-	-	60	82
4	2a	-	Benzil	-	90	89
5	2b	-	4,4-Dimethylbenzil	-	90	81
6	2c	-	9,10-Phenanthrenequinone	-	60	78
7	3a	-	-	Acetone	180	84
8	3b	-	-	Butan-2-one	180	86
9	3c	-	-	Acetophenone	120	82

1a: 2-(2-chlorophenyl)-1*H*-benzo[*d*]imidazole

1c: 2-(4-fluorophenyl)-1*H*-benzo[*d*]imidazole

2b: 2,3-dip-*tolyl*quinoxaline

3a: 2,3-dihydro-2,2,4-trimethyl-1*H*-benzo[*b*][1,4]diazepine

3c: 2,3-dihydro-2-methyl-2,4-diphenyl-1*H*-benzo[*b*][1,4]diazepine

1b: 2-*o*-tolyl-1*H*-benzo[*d*]imidazole

2a: 2,3-diphenylquinoxaline

2c: dibenzo[*a,c*]phenazine

3b: 2,4-diethyl-2,3-dihydro-2-methyl-1*H*-benzo[*b*][1,4]diazepine

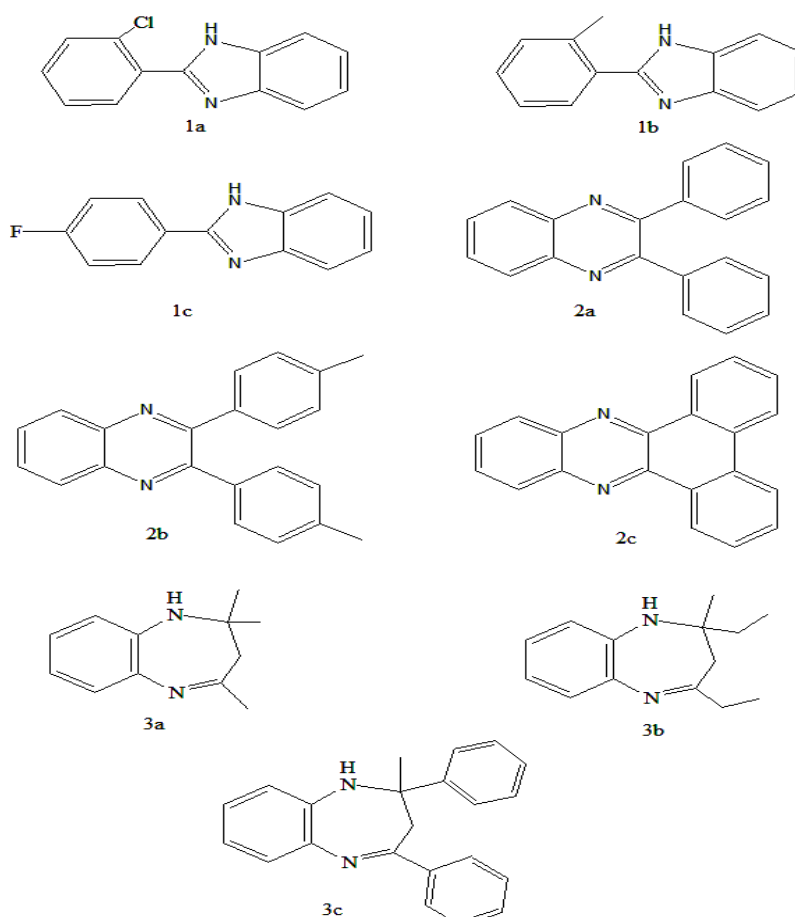
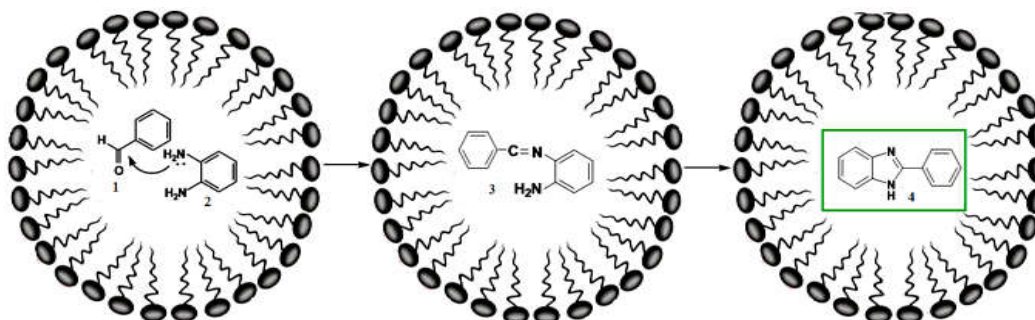
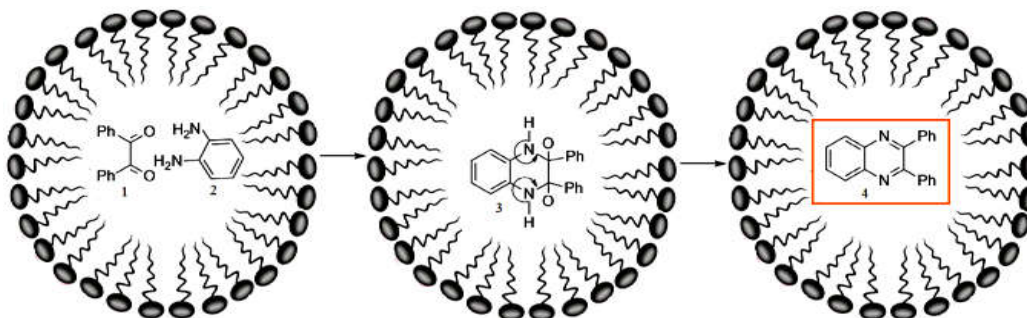


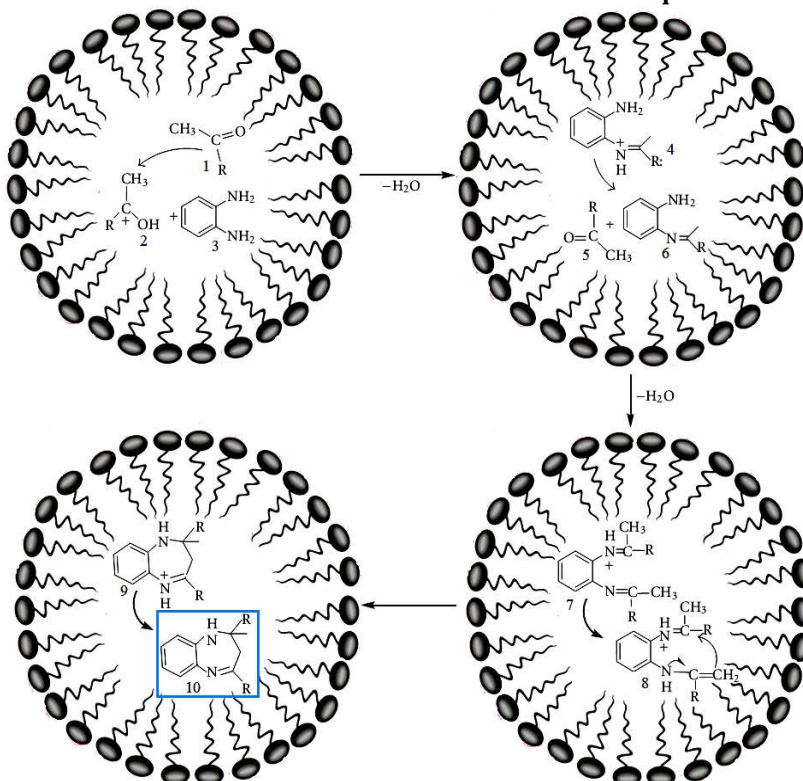
Figure 1. Structures of synthesized 1*H*-benzo[*d*]imidazoles (1a-1c), quinoxalines (2a-2c) and 2,3-dihydro-1*H*-benzo[*b*][1,4]diazepines (3a-3c)



Scheme 4. Plausible mechanism for the formation of 1*H*-benzo[*d*]imidazoles



Scheme 5. Plausible mechanism for the formation of quinoxalines



Scheme 6. Plausible mechanism for the formation of 2,3-dihydro-1*H*-benzo[*b*][1,4]diazepines

Characterization of Synthesized Compounds

Table 1, Entry 1: 2-(2-chlorophenyl)-1*H*-benzo[*d*]imidazole (1a)

¹H NMR (CDCl₃, 400 MHz): δ (ppm) 6.9-7.3 (m, 4H), 7.5-8.0 (m, 4H), 8.15 (s, 1H, NH).

Table 1, Entry 2: 2-*o*-tolyl-1*H*-benzo[*d*]imidazole (1b)

¹H NMR (CDCl₃, 400 MHz): δ (ppm) 1.3 (s, 3H), 6.85-7.45 (m, 4H), 7.9-8.2 (m, 4H), 8.3 (s, 1H, NH).

Table 1, Entry 3: 2-(4-fluorophenyl)-1*H*-benzo[*d*]imidazole (1c)

¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.2-7.75 (m, 4H), 8.2-8.35 (m, 4H), 8.4 (s, 1H, NH).

Table 1, Entry 4: 2,3-diphenylquinoxaline (2a)

¹H NMR (DMSO, 400 MHz): δ (ppm) 7.1- 7.55 (m, 10H), 7.65 -7.8 (m, 4H).

Table 1, Entry 5: 2,3-dip-tolylquinoxaline (2b)

¹H NMR (DMSO, 400 MHz): δ (ppm) 2.2 (s, 6H), 7.2- 7.6 (m, 8H), 7.7 -8.1 (m, 4H).

Table 1, Entry 6: dibenzo[*a,c*]phenazine (2c)

¹H NMR (DMSO, 400 MHz): δ (ppm) 7.4-7.85 (m, 4H), 8.2- 8.9 (m, 8H).

Table 1, Entry 7: 2,3-dihydro-2,2,4-trimethyl-1*H*-benzo[*b*][1,4]diazepine (3a)

¹H NMR (CDCl₃, 400 MHz): δ (ppm) 1.2 (s, 6H), 2.35 (s, 2H), 2.6 (s, 3H), 3.25 (br s, 1H, NH), 6.8-7.45 (m, 4H).

Table 1, Entry 8: 2,4-diethyl-2,3-dihydro-2-methyl-1*H*-benzo[*b*][1,4]diazepine (3b)

¹H NMR (CDCl₃, 400 MHz): δ (ppm) 1.2 (t, 3H), 1.5 (t, 3H), 1.8 (q, 2H), 2.3 (m, 2H), 2.6 (s, 3H), 2.85 (q, 2H), 3.4 (br s, 1H, NH), 6.9-7.55 (m, 4H).

Table 1, Entry 9: 2,3-dihydro-2-methyl-2,4-diphenyl-1*H*-benzo[*b*][1,4]diazepine (3c)

¹H NMR (CDCl₃, 400 MHz): δ (ppm) 1.65 (s, 3H), 2.5 (m, 2H), 3.3 (br s, 1H, NH), 6.7-7.55 (m, 10H), 7.75-8.1 (m, 4H).

CONCLUSION

In conclusion, a simple, mild and convenient synthetic procedure has been developed for the synthesis of 1*H*-benzo[*d*]imidazoles, quinoxalines and 2,3-dihydro-1*H*-benzo[*b*][1,4]diazepines. In this method, ammonium lauryl sulfate, an anionic surfactant proved to be an efficient catalyst for the synthesis of above compounds at room temperature using water as a solvent. Method provides green synthetic approach in terms of cost effectiveness of catalyst as well as solvent, easy workup and short reaction time affording high yield of the products.

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REFERENCES

- Anastas PT, Warner JC (1998). Green Chemistry: Theory and Practice. Oxford University Press, Oxford.
- Anastas PT (1999). Green Chemistry and the Role of Analytical Methodology Development. Crit. Rev. Anal. Chem. 29: 167-175.
- Namiesnik J (2000). Trends in Environmental Analytics and Monitoring. Crit. Rev. Anal. Chem. 30: 221-269.
- Armenta S, Garrigues S, Guardia MDL (2008). Green Analytical Chemistry. Trends Anal. Chem. 27: 497-511.
- Koel M, Kaljurand M (2006). Application of the Principles of Green Chemistry in Analytical Chemistry. Pure Appl. Chem. 78: 1993-2002.
- Tobiszewski M, Mechlinska A, Namiesnik J (2010). Green Analytical Chemistry -Theory and Practice. Chem. Soc. Rev. 39: 2869-2878.
- Dichiarante V, Ravelli D, Albini A (2010). Green Chemistry: State of the Art through an Analysis of the Literature. Green Chem. Lett. Rev. 3(2): 105-113.
- Galuszka A, Migaszewski Z, Namies J (2013). The 12 Principles of Green Analytical Chemistry and the Significance Mnemonic of Green Analytical Practices. Trends Anal. Chem. 50: 78-84.
- Saini MS, Kumar A, Dwivedi J, Singh R (2013). A Review: Biological Significances of Heterocyclic Compounds. Int. J. Pharma. Sci. Res. 4(3): 66-77.
- Gellis A, Kovacic H, Boufatah N, Vanelle P (2008). Synthesis and Cytotoxicity Evaluation of some Benzimidazole-4,7-diones as Bioreductive Anticancer Agents. Eur. J. Med. Chem. 43: 1858-1864.
- Ingle RG, Magar DD (2011). Heterocyclic Chemistry of Benzimidazoles and Potential Activities of Derivatives. Int. J. Drug. Dev. Res. 1(1): 26-32.
- Kalyankar TM, Pekamwar SS, Wadher SJ, Tiprale PS, Shinde GH (2012). Review on Benzimidazole Derivative. IJCPA. 3(4): 1-10.
- Lindsley CW, Zhao Z, Leister WH, Robinson RG, Barnett SF, Defeo-Jones D, Jones RE, Hartman GD, Huff JR, Huber HE, Duggan ME (2005). Allosteric Akt (PKB) Inhibitors: Discovery and SAR of Isozyme Selective Inhibitors. Bioorg. Med. Chem. Lett. 15: 761-764.
- Seitz LE, Suling WJ, Reynolds RC (2002). Synthesis and Antimycobacterial Activity of Pyrazine and Quinoxaline Derivatives. J. Med. Chem. 45: 5604-5606.
- He W, Myers MR, Hanney B, Spada AP, Bilder G, Galzcinski H, Amin D, Needle S, Page K, Jayyosi Z, Perrone MH (2003). Potent Quinoxaline-based Inhibitors of PDGF Receptor Tyrosine Kinase Activity Part 2: The Synthesis and Biological Activities of RPR127963 an Orally Bioavailable Inhibitor. Bioorg. Med. Chem. Lett. 13: 3097-3100.
- Baun JRD, Pallos FM, Baker DR (1977). "5-furoy l- 2,2,4-trimethy l-1,4-dihydro-1*H*-1,5-benzodiazepine as an Anti-Inflammatory Agent". Chemical Abstracts. 86: 5498d.
- Schultz H (1982). Benzodiazepines. Springer, Heidelberg, Germany.

- Smiley RK (1979). *Comprehensive Organic Chemistry*. Pergamon, Oxford, U K.
- Landquist JK (1984), *Comprehensive Heterocyclic Chemistry*. vol 1, Pergamon, Oxford, UK.
- Randall LO, Kappel B (1973). "Pharmacological Activity of Some Benzodiazepines and Their Metabolites". In *Benzodiazepines*, Garattini S, Mussini E (eds) Raven, New York, NY, USA.
- Scholl H, Kloster G, Stocklin, G (1983). Bromine-75-Labeled 1,4-Benzodiazepines: Potential Agents for the Mapping of Benzodiazepine Receptors in vivo : Concise Communication. *J. Nucl. Med.* 24: 417-422.
- Sharma S, Gangal S, Rauf A (2008). Green Chemistry Approach to the Sustainable Advancement to the Synthesis of Heterocyclic Chemistry. *Rasayan J. Chem.* 4(1): 693-717.
- Shinde PV, Kategaonkar AH, Shingate BB, Shingare MS (2011). Surfactant Catalyzed Convenient and Greener Synthesis of Tetrahydrobenzo[a]xanthene-11-ones at Ambient Temperature. *Beilstein J. Org. Chem.* 7: 53–58.

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