Gurukul International Multidisciplinary Research Journal (GIMRJ)*with* International Impact Factor 8.357
Peer Reviewed Journal
https://doi.org/10.69758/GIMRJ/2504I5VXIIIP0052

e-ISSN No. 2394-8426
Monthly Issue
APR-2025
Issue–IV, Volume–XIII

KPS as an Eco-Friendly Oxidant for synthesis of dibenzo [b, e] [1,4] diazepine derivatives through intermolecular radical cyclization in aqueous solution

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ABSTRACT:

Bio active dibenzo [b, e] [1,4] diazepine derivatives have been synthesised by Potassium Persulfate as an eco-friendly oxidant for Oxidative Transformations. This type of reaction likely involves the nucleophilic attack of the amine group on the carbonyl group of the aldehyde, followed by cyclization to form the diazepine ring. This kind of reaction is particularly useful in creating complex heterocyclic structures, which are important in the development of biologically active compounds. Dibenzo [b, e] [1,4] diazepine derivatives were efficiently and easily synthesised by addition/cyclisation of compounds o-phenylenediamine with substituted o-Chloro benzaldehyde, K_2CO_3over KPS (25 mol%)with high efficiency in water as a green solvent at 80 °C. The synthesized compounds were characterized by ^1H NMR, Mass and IR spectral analysis.

Keywords: KPS [Potassium persulfate], K_2CO_3, dibenzo [b,e] [1,4] diazepine derivatives ,substituted aromatic aldehydes,*o*-phenylenediamine(OPD).

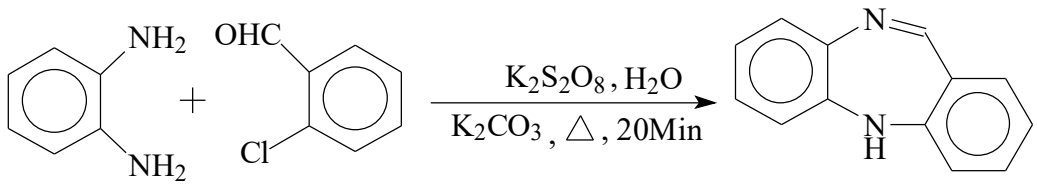
I. INTRODUCTION:

Benzodiazepines are highly important in both medicinal chemistry and clinical practice due to their wide range of therapeutic effects. Their ability to treat a variety of disorders, such as epilepsy (anti-convulsant),Long-Term Insomnia Treatment with Benzodiazepines and Alzheimer's Disease, depression (anti-depressive), anxiety (anti-anxiety), and inflammation (anti-inflammatory), along with their sedative, tranquilizing, and analgesic properties[1,2]., makes them valuable in both clinical and industrial applications. Moreover, their role in cardiovascular treatment[3] and their applications in fine chemical industries, such as in the preparation of photographic dyes, shows their versatility[4]. The fact that benzodiazepines can serve as synthons for the preparation of fused-ring compounds like triazolo, oxadiazolo, and oxazino derivatives further expands their significance, particularly in the development of novel compounds with potentially enhanced or diverse activities5. They serve as valuable intermediates in organic synthesis. Their structural versatility allows for the creation of various bioactive compounds, which can be used in the development of new drugs or materials.

Keeping in view this broad spectrum of biological activity associated with these compounds various synthetic route has been reported in the literature, these include condensation of *o*-phenylenediamine with *α-β* unsaturated carbonyl compounds[6], *β*-haloketones[7] or ketones in the presence various catalyst such as copper-bronze [8],$Hg(OTf)_2$[9], $ZnCl_2$[10], CAN[11], ionic liquid[12-13], zinc montmorillonite as catalyst at r.t[14] , $AgNO_3$[15], $Ag_3PW_{12}O_{40}$[16], solid super acid sulfated zirconia[17], amberlyst-15[18], sodium dodecyl sulfate[19], acetic acid- under MWI[20], citric acid[21], $Yb(OTf)_3$ [22],MgO-POCl3 [23],TBAB[24],PPA-SiO_2[25], $NaBH_4$[26] BF_3OEt[27]however, despite the potential utility of these catalysts, a limitation with the majority of benzodiazepine derivatives syntheses is that of tedious workup procedure, formation of side products, involve long reaction time, give low yield of products and use expensive reagents. Furthermore, very few polycyclic bioactive benzodiazepines are reported in the literature.a benzodiazepine bio isostere, has just been validated in tablet as solid material by the use of spectrophotometric determination[28]. On the

basis of these findings and our ongoing research program on the synthesis and search of green protocol for the synthesis of bioactive heterocyclic compounds[11], we became interested in designing compounds like dibenzo [b, e] [1,4] diazepine derivatives with potentially improved novel activities.

The KPS [Potassium persulfate] mediated condensation and intermolecular cyclization with K_2CO_3 was initially attempted. No reaction was observed without use of K_2CO_3 and KPS.



1 2 3(a-h)

Scheme: Synthesis of dibenzo [b, e] [1,4] diazepines by$K_2S_2O_8$-mediated radical cyclization

II. METHODS AND MATERIAL:

All ^{1}H NMR spectra were recorded in $CDCl_3$ on a Brucker AC 200 and Brucker MSL 300spectrometers and chemical shift were reported in ppm downfield from tetra methyl silane.
Infrared spectra were recorded on a Perkin Elmer infra-red spectrophotometer using KBr discs and Mass spectra were taken on ESI–Esquire 3000 Brukers Daltonics instrument, TLC was performed on silica gel coated aluminium plates using ethyl acetate and pet ether (3:7 v/v) as eluent, melting points were determined on an electronic melting point apparatus and were uncorrected.

General procedures for the synthesis of Dibenzo[b,e][1,4]diazepine derivatives 3(a-h):

A mixture of *o*-phenylenediamine (10 mmole), substituted benzaldehydes (10 mmole), KPS (25 mol %) and Potassium carbonate (10 mmole) were dissolved in H_2O (20 ml), was heated at 80 °C for the stipulated time. The progress of the reaction is monitored by TLC. After completion of the reaction, the corresponding product was obtained through simple filtering, and the crude solid residue recrystallized from ethanol,further the resulting residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate as eluent to afford the desired products dibenzo[b,e][1,4]diazepines in excellent yield.

Spectral data of the selected products:

3b: IR (KBr): 3389, 2970, 1631,1591,1470,1100,744 cm-1; 1HNMR (CDCl3): δ= 3.4 (brs,1H), 6.1-7.1 (m, 9H); MS (m/z):194 (M+)

3d: IR (KBr): 3389, 2970, 1731,1581,1460,1100,744 cm-1; 1HNMR (CDCl3): δ= 3.5 (brs,1H), 6.5-7.0 (m, 11H); MS (m/z):324 (M+)

3e: IR (KBr): 3389, 2922, 1600, 1356,746 cm-1; 1HNMR (CDCl3): δ= 2.5 (s, 3H) 3.6 (brs,1H), 6.0-7.5 (m, 8H); MS (m/z): 208 (M+)

3g: IR (KBr): 3377, 1664, 1599, 1440,750 cm-1; 1HNMR (CDCl3): δ= 2.2 (s, 6H), 3.4 (brs,1H), 6.1-7.3(m, 7H); MS (m/z):222 (M+).

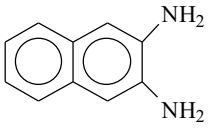
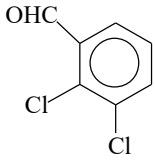
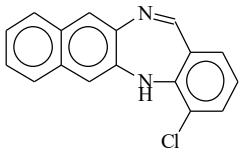
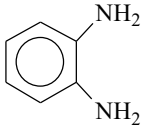
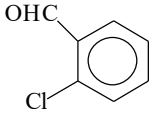
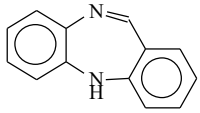
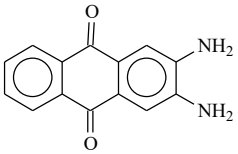
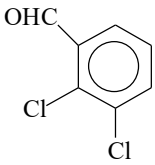
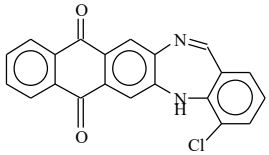
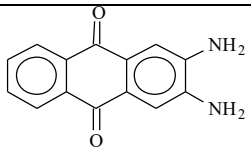
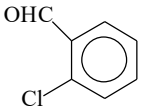
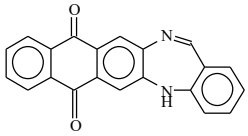
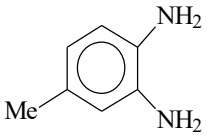
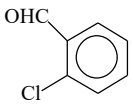
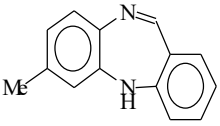
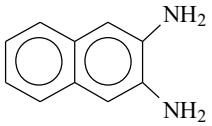
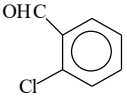
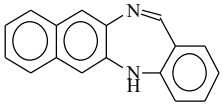
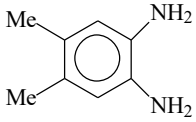
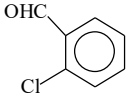
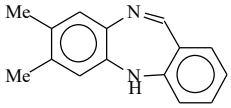
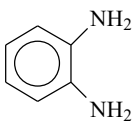
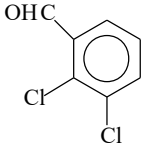
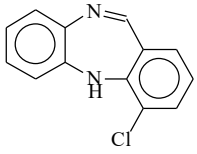
3h: IR (KBr): 3390, 2950, 1650,1590,1470,1100,744 cm-1;1HNMR (CDCl3): δ=3.5 (brs,1H), 6.0-6.9 (m, 8H); MS (m/z): 228 (M+)

III. RESULTS AND DISCUSSION

In the current strategy, the synthesis of dibenzo[b,e][1,4]diazepine derivatives from *o*-phenylenediamine has been carried out successfully with substituted benzaldehydes in the presence of KPS along with K_2CO_3, cleaner transformation obtained, the progress of the reaction was monitored by TLC. The products

were obtained in excellent yield, the characterization of the synthesized compounds has been carried out by IR, ^{1}H-NMR and Mass spectroscopy data, the results are summarized in Table, the products are known compounds and were confirmed by comparison of their physical and spectral data with authentic samples[8].

Table: KPS mediated Synthesis of dibenzo (b, e) (1, 4) diazepine derivatives3(a-h)

Entry	Phenylenediamine	Aldehydes	Products	Yields (%)	M.P
a				85	192-194
b				86	96-98
c				85	269-271
d				82	274-276
e				82	93-95
f				86	199-201
g				85	113-115
h				86	99-101

IV. CONCLUSION:

In summary, we have developed a simple, environmentally benign and mild synthetic method to afford dibenzo[b,e][1,4]diazepine derivatives with KPS and K_2CO_3in quantitative. Noteworthy, $K_2S_2O_8$ is used as the major oxidant in the creation of a variety of C − C/C − N/C − S/C − O bonds, allowing access to a variety of cyclic and acyclic compounds. In the process of oxidation $S_2O_8^{2-}$ is either directly involved or the radical anion sulphate (SO_4^-), which, in turn, is produced by the breakdown of $K_2S_2O_8$[29]. Observations highlight that KPS is good oxidant for oxidative preparation of dibenzo[b,e][1,4]diazepine that changes the state and reactivity of *o*-phenylenediamine and substituted aromatic aldehydes with K_2CO_3 in aqueous medium in short reaction time to afford82-86% yield.

V. ACKNOWLEDGEMENT:

Authors would like to thanks the Principals, Maulana Azad College of Arts, Science & Commerce, Aurangabad and the Principals of Milliya Arts, Science & Management Science College, Beed for providing necessary support and facility to carry out this research work.

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