

Copper-Bronze Catalyst: An Efficient Green Approach for the Synthesis of Dibenzo[b,e][1,4]diazepine Derivatives

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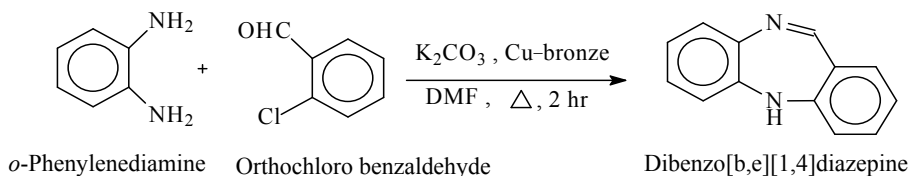
Abstract: Dibenzo[b,e][1,4]diazepine derivatives medicinally important hetero systems have been synthesized by green, efficient and convenient synthesis involving Cu-bronze as a novel catalyst by condensation of *o*-phenylenediamine with aromatic aldehydes. This method is advantageous because of high yield of product easy workup procedure. The synthesized compounds were characterized by ¹H NMR, Mass and IR spectral analysis.

Keywords: Cu-bronze, Dibenzo[b,e][1,4]diazepine derivatives, *o*-phenylenediamine, substituted aromatic aldehydes.

Introduction

In the field of organic chemistry, an important largest area of research has been occupied by heterocyclic compounds. Synthesis of *N* containing heterocyclic compounds especially several type of benzodiazepine derivatives have been provoked much interest due to reported broad spectrum of biological activities such as anti-convulsant, anti-depressive, anti-bacterial, anti-anxiety, anti-inflammatory, tranquilizing, analgesic, hypnotic and sedative agents^{1,2}. Benzodiazepines play a leading role in the treatment of cardiovascular disorder³. Additionally they have application in fine chemical industries such as photographic dyes for acrylic fiber⁴. Also have been reported to be used as a valuable synthons for the synthesis of fused ring benzodiazepines class of compounds like triazolo, oxadiazolo, oxazino and furanobenzodiazepines⁵. Keeping in view this broad spectrum of biological activity associated with these compounds various synthetic route have been reported in the literature, these include condensation of *o*-phenylenediamine with α - β unsaturated carbonyl compounds⁶, β -haloketones⁷ or ketones in the presence various catalyst such as BF₃OEt⁸, NaBH₄⁹, PPA- SiO₂¹⁰, TBAB¹¹, MgO-POCl₃¹², Yb(OTf)₃¹³, citric acid¹⁴, amberlyst-15¹⁵, sodium dodecyl sulfate¹⁶, Ag₃PW₁₂O₄₀¹⁷, solid super acid sulfated zirconia¹⁸, acetic acid- under MWI¹⁹, AgNO₃²⁰, zinc montmorillonite as catalyst at r.t²¹, ionic liquid^{22, 23}, CAN²⁴, ZnCl₂²⁵ and Hg(OTf)₂²⁶. 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. Further more, very few polycyclic bioactive benzodiazepines are reported in the literature. On the basis of these findings and our continuing research program on the synthesis and search of green catalyst for the synthesis of bioactive interesting heterocycles.¹¹ We became interested and designed a green approach for the synthesis of biologically active dibenzo[b,e][1,4]diazepine derivatives. To the best of our knowledge, copper-bronze catalyst for the synthesis of dibenzo diazepine derivatives has not been reported in the literature.



Scheme 1. Synthesis of Dibenzo[b,e][1,4]diazepines

The copper-bronze catalyzed condensation and intramolecular cyclization was initially attempted and Buchwald's condition²⁷ for intramolecular *N*-arylation reactions were investigated. No reaction was observed without use of catalyst.

Experimental

All ¹H NMR spectra were recorded in CDCl₃ on a Bruker AC 200 and Bruker MSL 300 spectrometers 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 aluminum 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), Cu-bronze (10 mol %) and potassium carbonate (2 equiv), refluxed for 2 h in 20 mL dimethyl formamide, the completion of reaction was monitored by TLC. After completion of reaction the reaction mixture was cooled and poured on crushed ice, extracted from ethyl acetate (20 mL) and washed with water and brine. The solvent was removed by distillation under reduced pressure to afford the products in 80-85% yield.

Spectral data of the selected products

3a: 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⁺)

3b: 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⁺)

3c: 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⁺)

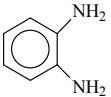
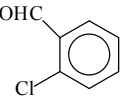
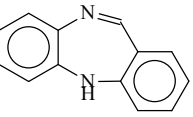
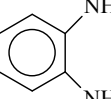
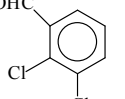
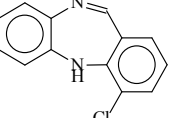
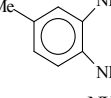
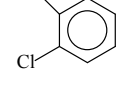
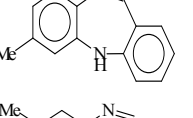
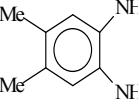
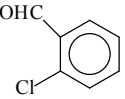
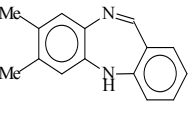
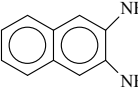
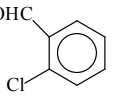
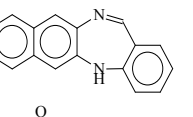
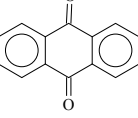
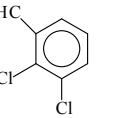
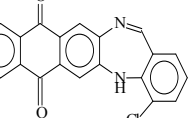
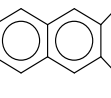
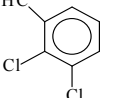
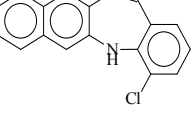
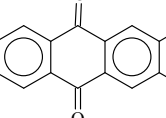
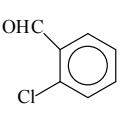
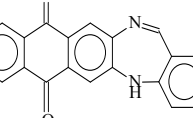
3d: IR (KBr): 3377, 1664, 1599, 1440,750 cm⁻¹; ¹HNMR (CDCl₃): δ= 2.2 (s, 6H), 3.4 (brs, 1H), 6.1-7.3(m, 7H); MS (m/z):222 (M⁺).

3h: IR (KBr): 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⁺)

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 copper-bronze and potassium carbonate, cleaner transformation obtained, the progress of the reaction was monitored by TLC. The substrate and catalyst is not reported earlier in the literature to the best of our knowledge. The products were obtained in excellent yield, the characterization of the synthesized compounds has been carried out by IR, ¹H-NMR and Mass spectroscopy data²⁸ and the results are summarized in Table 1.

Table 1. Cu-bronze catalyzed synthesis of dibenzo[b,e][1,4]diazepine derivatives **3(a-h)**

Entry	Phenylenediamine	Aldehydes	Products	Yield, %	M.P
a				80	94-96
b				85	98-99
c				82	92-93
d				84	112-113
e				82	198-199
f				82	268-269
g				85	190-191
h				82	272-274

Conclusion

We have developed a simple and convenient, environmentally benign, mild synthetic method to afford dibenzo[b,e][1,4]diazepine derivatives with green catalyst under reflux conditions in quantitative yields. To the best of our knowledge, it is probably first example of synthesizing dibenzo[b,e][1,4]diazepine derivatives by using copper-bronze as a catalyst. The simplicity of the method, the ease of the product formation in short reaction time, yield of the product is good.

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