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1,3-dibromo-5,5-dimethylhydantoin (DBH): A novel and efficient catalyst for the synthesis of quinoxaline derivatives under solvent-free conditions

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ABSTRACT

1,3-Dibromo-5,5-dimethylhydantoin (DBH) was found to be an effective catalyst for the condensation of 1,2-diamines with 1,2-dicarbonyl compounds to afford the corresponding quinoxaline derivatives in excellent yields under mild reaction conditions.

KEYWORDS

1,3-Dibromo-5,5-dimethylhydantoin (DBH);
Quinoxaline derivatives;
1,2-Diamines;
1,2-Dicarbonyl compounds.

INTRODUCTION

Quinoxaline derivatives are an important class of benzoheterocycles[1], which have a wide range of biological and pharmacological activity[2]. They have been widely used as anticarcinogen[3], antimicrobial[4], antihelmintic[5], HIV-1 reverse transcriptase inhibitor[6], and pesticide[7]. Moreover, they also serve as building blocks in the synthesis of organic semiconductors[8], rigid subunits in macrocyclic receptors or for molecular recognition[9], dyes[10], and electroluminescent materials[11]. In recent years, the synthesis of quinoxalines has attracted considerable attention[12] and a wide range of synthetic methods has been developed for the synthesis of quinoxaline derivatives[13]. The conventional synthetic methods of quinoxaline derivatives were carried out in organic solvent via the condensation of arene-1,2-diamines with 1,2-dicarbonyl compounds for 2-12 hours under refluxing conditions with the yields of 34-85%[14], or in high boiling point solvent such as dimethylsulfoxide (DMSO) using the molecular iodine as the catalyst[15]. A number of catalysts have been developed for the preparation of quinoxalines, including Bi^{3+}[16], MnO_2[17], $POCl_3$[18], $Ga(OTf)_3$[19], cerium ammonium nitrate[20], $CuSO_4.5H_2O$[21], AcOH[22] or $RuCl_2$-$(PPh_3)_3$[23] as well as SA/MeOH[24]. Very recently, other catalysts, such as metal hydrogen sulfates[25], $CuCl_2$ combined with molecular sieve[26] and molybdophosphoric acid exchanged by iron[27]. However, most of the existing methodologies suffer from one or more limitations such as complicated reaction process, expensive and detrimental metal catalysts, using of volatile organic solvents, low product yields, and harsh reaction conditions, which come into collision with both economical and environmental requirements. Due to these disadvantages, the search for new catalysts which are green and cheaper remains an existing challenge. Although great success has been obtained, many of these processes suffer from drawbacks such as drastic reaction conditions, low product yields, tedious work-up procedures, using toxic metal salts as catalysts, long reaction time and rela-

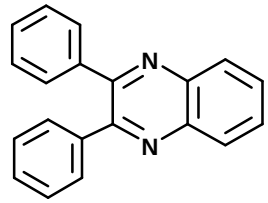
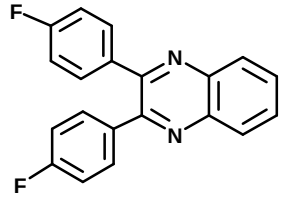
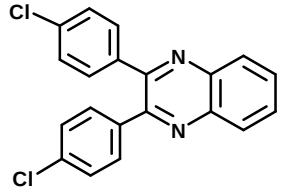
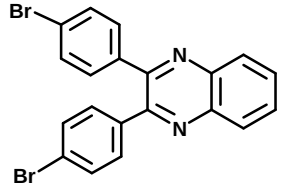
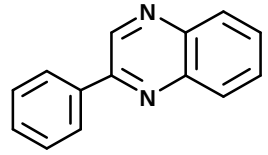
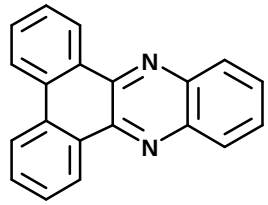
tively expensive reagents. Hence, the search for the better method, especially the readily available and green catalysts, is still being actively pursued.

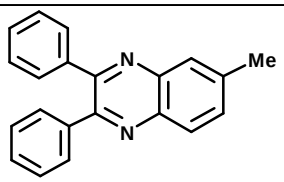
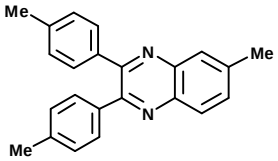
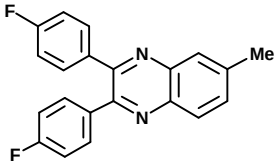
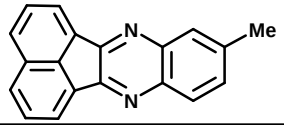
RESULTS AND DISCUSSION

In continuation of our on-going research on various transformations by halogenating agents[28-34], herein we reported the use of DBH as a more robust and efficient catalyst for the one-pot synthesis of the quinoxalines derivatives 3a–o by reaction of 1,2-dicarbonyl compounds with different 1,2-diamines in excellent yields (90%–96%) under solvent free conditions (Scheme 1, TABLE 1).

Scheme 1

TABLE 1 : Synthesis of quinoxalines using different 1,2-diamines and 1,2-diketones by DBH

Entry	Product [a]	Time (min)	Yield (%)[b]	Mp (°C)
3a		30	95	129–131
3b		28	90	133–135
3c		31	92	192–194
3d		27	90	187–189
3e		31	91	77–78
3f		30	93	117–119

Entry	Product [a]	Time (min)	Yield (%)[b]	Mp (^{o}C)
3g		34	95	138–139
3h		31	90	140–142
3i		28	91	165–166
3j		30	96	233–234

As shown in TABLE 1, the reactions were completed within 27–34 min under solvent free conditions. The experimental results indicate that the most effective conversion occurred when a mole ratio of 1:0.12 substrate/DBH was used. Longer reaction times were required when lower amounts of DBH were employed. It is important to note that no quinoxalines derivatives were afforded when the reactions were performed in the absence of DBH in the reaction mixture.

The advantages or the characteristic aspects of the method described in this paper in comparison with other previously reported ones include: the yields of products were better than the previously reported yields and in addition, the catalyst DBH is inexpensive and moisture stable and no special measures are required for the reaction.

EXPERIMENTAL

The employed chemicals were obtained from either Merck or Fluka and used as received unless otherwise noted. The IR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and the NMR spectra were obtained in CDCl3 using a 90 MHz JEOL FT NMR spectrometer. All the melting points were determined on a Büchi 530 melting point apparatus and are reported uncorrected.

Typical experimental procedure is as follows: a mixture of 1,2-diketone (2 mmol), 1,2-diamine (2 mmol) and 1,3-dibromo-5,5-dimethyl hydantoin (DBH) (0.12 mmol, 0.34 mg) was stirred in an oil-bath at 110 ^{0}C. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was directly with ethyl acetate. The upper layers were decanted, combined, dried over anhydrous $MgSO_4$ and was concentrated under *vacuo* to afford the crude product. The product was recrystallized from acetone or puriûed by column chromatography on silica gel using petroleum ether–ethyl acetate as the eluent to give the analytically pure product. The desired pure product(s) was characterized by comparison of their physical data with those of known quinoxalines[16-24].

CONCLUSIONS

The present methodology shows that 1,3-dibromo 5,5-dimethyl hydantoin (DBH) is an efficient catalyst in the one-pot synthesis of quinoxalines derivatives. The main advantages of the presented protocol are mild, clean and environmentally benign reaction conditions, as well as the high yields. Furthermore, this method is also expected to find application in organic synthesis due to the low cost of the catalyst. It is believed that this method will be a useful addition to modern synthetic methodologies.

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REFERENCES

[1] S.Gozyo, M.Kenji, K.Yoshihisa; Heterocycles, **27**, 2481 **(1988)**.
[2] P.Corona, M.Loriga, P.M.Costi, S.Ferrari, G.Paglietti; Eur.J.Med.Chem., **43**, 189 **(2008)**.
[3] P.Haldar, B.Dutta, J.Guin, J.K.Ray; Tetrahedron Lett., **48**, 5855 **(2007)**.
[4] Z.J.Zhao, W.H.Leister, R.G.Robinson, S.F.Barnett, D.Defeo-Jones, R.E.Jones, G.D.Hartman, J.R.Huff, H.E.Huber, M.E.Duggan, C.W.Lindsley; Bioorg. Med.Chem.Lett., **15**, 905 **(2005)**.
[5] S.Y.Hassan, S.N.Khattab, A.A.Bekhit, A.Amer; Bioorg.Med.Chem.Lett., **16**, 1753 **(2006)**.
[6] J.Balzarini, E.D.Clercq, A.Carbonez, V.Burt, J.P.Kleim; AIDS Res.Hum.Retrov., **16**, 517 **(2000)**.
[7] X.Hui, J.Desrivot, C.Bories, P.M.Loiseau, X.Franck, R.Hocquemiller, B.Figadère; Bioorg.Med.Chem. Lett., **16**, 815 **(2006)**.
[8] S.Dailey, W.J.Feast, R.J.Peace, I.C.Sage, S.Till, E.L.Wood; J.Mater.Chem., **11**, 2238 **(2001)**.
[9] T.Mizuno, W.H.Wei, L.R.Eller, J.L.Sessler; J.Am. Chem.Soc., **124**, 1134 **(2002)**.
[10] S.A.Kotharkara, D.B.Shinde; Bioorg.Med.Chem. Lett., **16**, 6181 **(2006)**.
[11] N.D.Sonawane, D.W.Rangnekar; J.Heterocycl. Chem., **39**, 303 **(2002)**.
[12] K.Niknam, D.Saberi, M.Mohagheghnejad; Molecules, **14**, 1915 **(2009)**.
[13] J.T.Hou, Y.H.Liu, Z.H.Zhang; J.Heterocycl.Chem., **47**, 703 **(2010)**.
[14] D.J.Brown; Quinoxalines: Supplement II in the Chemistry of Heterocyclic Compounds, E.C.Taylor, P.Wipf, (Eds); John Wiley and Sons: New Jersey, **(2004)**.
[15] R.S.Bhosalea, S.R.Sardaa, S.S.Ardhapurea, W.N.Jadhava, S.R.Bhusareb, R.P.Pawar; Tetrahedron Lett., **46**, 7183 **(2005)**.
[16] S.Antoniottia, E.Duñach; Tetrahedron Lett., **43**, 3971 **(2002)**.
[17] S.A.Raw, C.D.Wilfred, R.J.K.Taylor; Chem. Commun., 2286 **(2003)**.
[18] C.Venkatesh, B.Singh, P.K.Mahata, H.Lla, H.Junjappa; Org.Lett., **7**, 2169 **(2005)**.
[19] J.J.Cai, J.P.Zou, X.Q.Pan, W.Zhang; Tetrahedron Lett., **49**, 7386 **(2008)**.
[20] S.V.More, M.N.V.Sastry, C.F.Yao; Green Chem., **8**, 91 **(2006)**.
[21] M.M.Heravi, S.Taheri, K.Bakhtiari, H.A.Oskooie; Catal.Commun., **8**, 211 **(2007)**.
[22] M.R.Islami, Z.Hassani; ARKIVOC, **15**, 280 **(2008)**.
[23] C.S.Cho, S.G.Oh; Tetrahedron Lett., **47**, 5633 **(2006)**.
[24] H.R.Darabi, S.Mohandessi, K.Aghapoor, F.Mohsenzadeh; Catal.Commun., **8**, 389 **(2007)**.
[25] K.Niknam, M.A.Zolfigol, Z.Tavakoli; J.Chin.Chem. Soc., **55**, 1373 **(2008)**.
[26] C.S.Cho, W.X.Ren; J.Organomet.Chem., **694**, 3215 **(2009)**.
[27] K.T.V.Rao, P.S.S.Prasad, N.Lingaiah; J.Mol.Catal. A: Chem., **312**, 65 **(2009)**.
[28] H.Ghasemnejad-Bosra, M.Faraje, S.Habibzadeh, F.Ramzaniyan-Lehmali; J.Serb.Chem.Soc., **75**, 299 **(2010)**.
[29] H.Ghasemnejad-Bosra; Heterocycles, **68**, 175 **(2006)**.
[30] D.Azarifar, H.Ghasemnejad-Bosra; Organic Chemistry: An Indian Journal, **8(8)**, 303 **(2012)**.
[31] D.Azarifar, H.Ghasemnejad-Bosra, M.Tajbaksh; J.Heterocycl.Chem., **44**, 467 **(2007)**.
[32] H.Ghasemnejad-Bosra, M.Haghdadi, I.Gholampour-Azizi; Heterocycles, **75**, 391 **(2008)**.
[33] H.Ghasemnejad-Bosra, M.Haghdadi, O.Khanmohamadi, M.Gholipour, G.Asghari; J.Chin.Chem.Soc., **55**, 464 **(2008)**.
[34] H.Ghasemnejad-Bosra, M.Faraje, S.Habibzadeh; Helv.Chim.Acta., **92**, 575 **(2009)**.