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PDTC - CATALYZED ONE-POT TWO-COMPONENT SYNTHESIS OF SUBSTITUTED-QUINOXALINES

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ABSTRACT
Potassium Dodecatungstocobaltate Trihydrate [PDTC, $K_5CoW_{12}O_{40}$-$3H_2O$] mediated an alternative method has been developed in excellent yields for the synthesis of a series of quinoxalines (3a-l) by one-pot two-component condensation reaction of *o*-phenylenediamine (1) and various 1,2-diketones (2) at RT in ethanol.
Keywords: PDTC, Substituted-Quinoxalines, Two-Component Condensation.
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INTRODUCTION

Quinoxaline derivatives are an important class of nitrogen-containing heterocycles in medicinal chemistry, possessing a wide and diverse spectrum of pharmacological properties,[2–6] such as anti-biotic, anti-viral,[7] anti-cancer,[8] and anti-inflammatory activities.[9–11] The quinoxaline core moiety is also associated with different applications in organic semiconductors,[12,13] dyes,[14] cavitands[15,16,] and dehydroannulenes.[17]

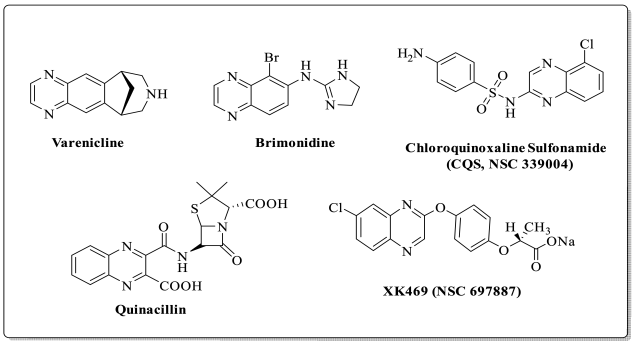

Fig.-1: Biologically Active Quinoxaline Molecules

In the studies towards the synthesis of new compounds as useful biologically active scaffolds, we report in this method an efficient synthesis of quinoxaline derivatives. Based on the literature survey, there was no report for the synthesis of quinoxalines using Potassium Dodecatungstocobaltate Trihydrate [PDTC, $K_5CoW_{12}O_{40}$-$3H_2O$], which is a heteropoly acid and an inexpensive, recyclable catalyst.[18-21] Because of this reason, we have investigated in depth the utility of Potassium Dodecatungstocobaltate Trihydrate for the synthesis of quinoxalines. In the present investigation, we have taken advantage of NH_2 and keto groups in a two-component condensation reaction of *o*-phenylenediamine (1) and 1,2-diketone (2) at room temperature in ethanol in the preparation of substituted-quinoxaline derivatives (Scheme-1).

EXPERIMENTAL

Material and Methods

To measure the melting points of the compounds, the Fischer-Johns melting point apparatus was used. Perkin Elmer-283B & Nicolet-740 was used to record IR spectra. Varian Gemini-200, Varian unit-500, and Avance 300 MHz, Avance 400 MHz, BrukerUx-NMR were used to record ^{1}H NMR spectra, and VG Micro mass 7070H (ESI was used to record Mass spectra).

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Typical Procedure for the Synthesis of Substituted-quinoxalines (3a-l)

The mixture of *o*-phenylenediamine (**1a**, 1.0 mmol), 1,2-diketone (**2a,** 1.1 mmol), and Potassium Dodecatungstocobaltate Trihydrate catalyst (10 mol%, 0.02 g) was stirred for 2.0 hr in 5 mL of EtOH at room temperature. After completion of the reaction, the solid catalyst was separated, washed with EtOH (2 x 5 mL), and the Potassium Dodecatungstocobaltate Trihydrate catalyst was dried. The filtrate was concentrated using Rotavapor, and the crude product was purified by column chromatography using a 2:8 ratio of EtOAc and hexane as eluent to get the following title compounds.

Representative Spectral Data

2,3-Diphenylquinoxaline (3a)

Yield: 87%.IR (KBr): υ3053, 1636, 1340, 766, 694 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.30-7.40 (m, 6H, Ar-H), 7.50 (m, 4H, Ar-H), 7.90 (dd, 2H, *J*=8.50 Hz, Ar-H), 8.20 (dd, 2H, *J*=9.0 Hz, Ar-H). ESI-MS: *m/z* = 283[M+H].

6-Chloro-3-methyl-2-phenylquinoxaline (3c)

Yield: 85%. IR (KBr): υ3063, 1607, 1509, 1245, 830,762 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.85 (s, 3H, $-CH_3$), 7.50-7.58 (m, 3H, Ar-H), 7.62-7.70 (m, 2H, Ar-H), 7.99 (d, 2H, *J*=9.0 Hz, Ar-H), 8.10 (d, 2H, *J*=8.55 Hz, Ar-H). ESI-MS: *m/z* = 255[M+H], 257 [M+2].

6-Chloro-2,3-di-p-tolyl phenyl quinoxaline (3e)

Yield: 86%. IR (KBr): υ 2920, 1640, 1334, 1057, 825 cm^{-1}. ^1H NMR ($CDCl_3$):δ 2.15 (s, 6H, 2x-CH_3), 7.15 (d, 4H, *J*=8.55 Hz, Ar-H), 7.40 (d, 4H, *J*=8.56 Hz, Ar-H), 7.68 (d, 1H, *J*=8.75 Hz, Ar-H), 8.05 (d, 1H, *J*=8.80 Hz, Ar-H), 8.14 (s, 1H, Ar-H). ESI-MS: *m/z* = 345[M+H], 347 [M+2].

2,3-Bis(4-methoxyphenyl)quinoxaline (3i)

Yield: 88%. IR (KBr): υ3006, 2838, 1607, 1509, 1245, 830,762 cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.85 (s, 6H, 2x -OCH_3), 6.88 (d, 4H, *J*=8.50 Hz, Ar-H), 7.50 (d, 4H, *J*=8.56 Hz, Ar-H), 7.70 (dd, 2H, Ar-H), 8.12 (dd, 2H, Ar-H). ESI-MS: *m/z* = 343[M+H].

6-Chloro-2,3-bis(4-fluorophenyl)quinoxaline (3k)

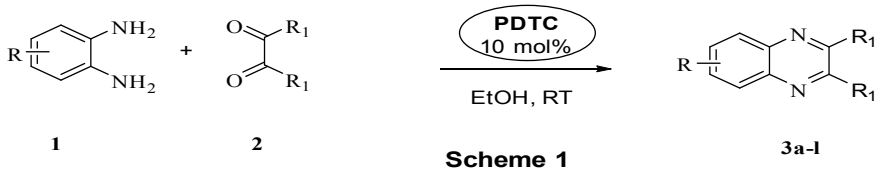
Yield: 80%. ^1H NMR ($CDCl_3$): δ 7.05 (dd, 4H, Ar-H), 7.50 (dd, 4H, Ar-H), 7.70 (d, 1H, *J*=8.75 Hz, Ar-H), 8.08 (d, 1H, *J*=8.75 Hz, Ar-H), 8.15 (s, 1H, Ar-H). ESI-MS: *m/z*=353[M+H], 355 [M+2].

6-Methyl-2,3-di-p-tolyl quinoxaline (3l)

Yield: 87%. IR (KBr): υ3029, 2914, 1616, 1338, 825 cm^{-1}. ^1H NMR ($CDCl_3$):δ 2.35 (s, 6H, 2x -CH_3), 2.60 (s, 3H, -CH_3), 7.10 (d, 4H, *J*=8.56 Hz, Ar-H), 7.40 (d, 4H, *J*=8.50 Hz, Ar-H), 7.58 (d, 1H, *J*=8.75 Hz, Ar-H), 7.90 (s, 1H, Ar-H), 8.05 (d, 1H, *J*=8.70 Hz, Ar-H). ESI-MS: *m/z* = 325[M+H].

RESULTS AND DISCUSSION

For a model experiment for the preparation of quinoxalines, the reaction between o-phenylenediamine and 1,2-bis(4-methoxyphenyl) ethane-1,2-dione was observed in the presence of 5, 10, 15 & 20 mol% of Potassium Dodecatungstocobaltate Trihydrate catalyst and ethanol, methanol, MeCN, and DMF as solvents at room temperature (Table-1).



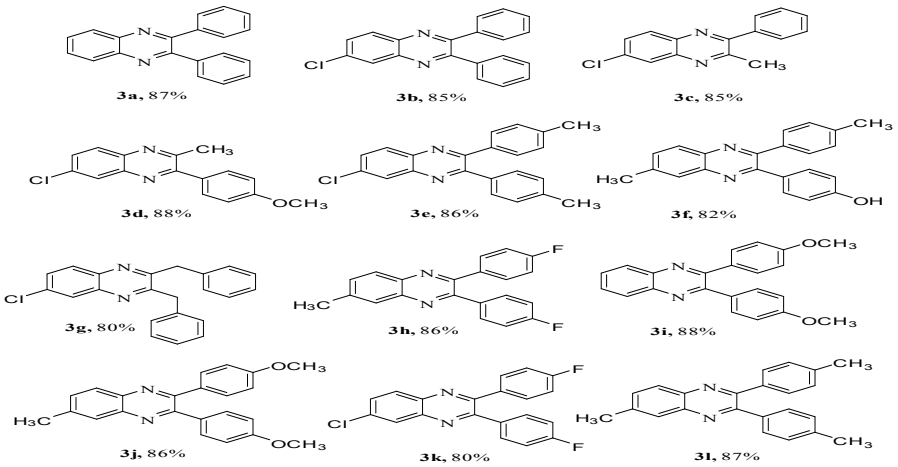
Scheme 1

Scheme-1: Synthesis of Substituted-Quinoxalines using PDTC Catalyst

The results indicated that using ethanol as a solvent with 5, 10, 15, and 20 mol% of Potassium Dodecatungstocobaltate Trihydrate catalyst at room temperature gave relatively good to excellent yields of the product in 2 h. However, using a higher amount of Potassium Dodecatungstocobaltate Trihydrate, there was no increase in the yield.

Table-1: Optimization of Catalyst for synthesis of 1,2-bis(4-methoxyphenyl)quinoxaline

Entry	Catalyst(mol%)	Time(h)	Yield(%)
1	$K_5CoW_{12}O_{40}.3H_2O$(5)	2.0	70
2	$K_5CoW_{12}O_{40}.3H_2O$(10)	2.0	88
3	$K_5CoW_{12}O_{40}.3H_2O$(15)	2.0	88
4	$K_5CoW_{12}O_{40}.3H_2O$(20)	2.0	88



Finally, we concluded that the best reaction condition is 10 mol% of Potassium Dodecatungstocobaltate Trihydrate with EtOH solvent at room temperature, resulting in 88% of isolated yield into quinoxaline. Thus, 10 mol% of Potassium Dodecatungstocobaltate Trihydrate catalyst with EtOH at room temperature was the choice for all the reactions (Scheme-1). We were able to recover and reuse the Potassium Dodecatungstocobaltate Trihydrate catalyst. Thus, the reaction of *o*-phenylenediamine and 1,2-diketone and Potassium Dodecatungstocobaltate Trihydrate catalyst (10 mol%) at room temperature afforded **3i** in 88% yield. After the completion of the reaction, the catalyst was recovered by filtration from the reaction mixture, thoroughly washed with ethanol, and reused for the same reaction to get **3i** in 88% yield under similar conditions. When we carried out repeated runs, there was not much reduction in the %yield (88 to 73) in the catalytic property (Table-2).

Table-2: Behaviour of reused catalyst for the synthesis of **3i**

Entry	0	1	2	3	4	5	6
Yield(%)	88	88	80	79	77	75	73

The above results showed that 10 mol% of Potassium Dodecatungstocobaltate Trihydrate catalyst is sufficient for the representative examples. For example, the compound 3i was confirmed by following spectral representation; the appearance of $[M+H]^+$ peak at *m/z*343 in mass spectrum, in IR C-H stretching at 2950 $cm^{-1}$for C=N stretching at 1607 cm^{-1} and six methoxy protons as singlet at δ 3.86 ppm, one doublet at 6.85 ppm (for 4H, Ar-H), one doublet at 7.50 ppm (for 4H, Ar-H) and the characteristic proton of quinoxalines at δ 7.75 & 8.25 ppm appearance in ^{1}H NMR. The generality and scope of this method was established with various 1,2-diketones and *o*-phenylenediamine, and the reaction proceeds very well. Good to excellent yields and shorter reaction times were noticed for other quinoxalines.

CONCLUSION

We have developed an alternative method for the one-pot two-component synthesis of substituted-quinoxalines **3a-l** by the condensation of various *o*-phenylenediamines and 1,2-diketones at RT using 10 mol% of Potassium Dodecatungstocobaltate Trihydrate catalyst. The present methodology shows very attractive features: shorter reaction times with excellent yields, followed by the catalyst recovery and reuse.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

The present work is related to *SDG-9: Industry, Innovation and Infrastructure*. All the authors contributed significantly to this manuscript, participated in reviewing/editing and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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REFERENCES

1. L. E. Seitz, W. J. Suling and R. C. Reynolds, *Journal of Medicinal Chemistry*, **45**, 5604(2002), http://doi.org/10.1021/jm020310n
2. M. M. Ali, M. M. F. Ismail, M. S. A. EI-Gabby, M. A. Zahran, and T. A. Ammar, *Molecules*, **5,** 864(2000), http://doi.org/10.3390/50600864
3. R. Sarges, H. R. Howard, R. C. Browne, L. A. Label, and P. A. Seymour, *Journal of Medicinal Chemistry*, **33,** 2240 (1990), http://doi.org/10.1021/jm00170a031
4. G. Arthur, K. B. Elor, G. S. Robssert, Z. Z. Guo, J. P. Richard, D. Stanley, R. K. John, and T. Sean, *Journal of Medicinal Chemistry*, **48,** 744 (2005), http://doi.org/10.1021/jm0492958
5. E. S. Lainne, J. S. William, and C. R. Robert, *Journal of Medicinal Chemistry*, **45,** 5604(2002), http://doi.org/10.1021/jm020310n
6. J. Andres, Z. Belen, A. Ibnacio, and M. Antonio, *Journal of Medicinal Chemistry*, **48,** 2019(2005), http://doi.org/10.1021/jm049952w
7. M. Loriga, S. Piras, P. Sanna e G. Paglietti, *Farmaco*, **52,** 157(1997).
8. C. W. Lindsley, Z. 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, and M. E. Duggan, *Bioorganic Medicinal Chemistry Letters*, **15,** 761(2005), http://doi.org/10.1016/j.bmcl.2004.11.011
9. G. Sakata, K. Makino and Y. Kurasawa, *Heterocycles*, **27,** 2481(1988), http://doi.org/10.3987/REV-88-397
10. W. He, M. R. Meyers, B. Hanney, A. Sapada, G. Blider, H. Galzeinski, D. Amin, S. Needle, K. Page, Z. Jayyosi, and H. Perrone, *Bioorganic Medicinal Chemistry Letters*, **13,** 3097(2003), http://doi.org/10.1016/S0960-894X(03)00655-3
11. Y. B. Kim, Y. H. Kim, J. Y. Park, and S. K. Kim, *Bioorganic Medicinal Chemistry Letters*, **14,** 541(2004), http://doi.org/10.1016/j.bmcl.2003.09.086
12. S. Dailey, J. W. Feast, R. J. Peace, I. C. Sage, S. Till and E. L. Wood, *Journal of Materials Chemistry*, **11**, 2238(2001), http://doi.org/10.1039/B104674H
13. D. O. Brien, M. S. Weaver, D. G. Lidzey and D. D. C. Bradley, *Applied Physical Letters*, **69**, 881(1996), http://doi.org/10.1063/1.117975
14. E. D. Brock, D. M. Lewis, T. I. Yousaf and H. H. Harper (The Procter & Gamble Company, USA *WO 9951688*) (1999); *Chemical Abstract*, **131,** 287743 (2000).
15. L. S. Jonathan, M. Hiromitsu, M. Toshihisa, M. L. Vincent, and F. Hiroyuki, *Journal of American Chemical Society*, **124,** 13474(2002), http://doi.org/10.1021/ja0273750
16. P. C. Peter, Z. Gang, A. M. Grace, H. Carlos, and M. G. T. Linda, *Organic Letters*, **6,** 333(2004), http://doi.org/10.1021/ol036045x
17. O. Sascha and F. Rudiger, *Synlett*, 1509 (2004), http://doi.org/10.1055/s-2004-822392
18. N. Mizuno, M. Misono, *Chemical Review*, **98,** 199(1998), http://doi.org/10.1021/cr960401q
19. L. C. W Baker, T. P. Mc Cutcheon, *Journal of the American Chemical Society,* **81,** 4503(1956), http://doi.org/10.1021/ja01599a001
20. L. C. W Baker, T. P. Mc Cutcheon, *Journal of American Chemical Society,* **84,** 4744 (1959).
21. J. Walmsley, *Journal of Chemical Education,* **69,** 936 (1992), http://doi.org/10.1021/ed069p936

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