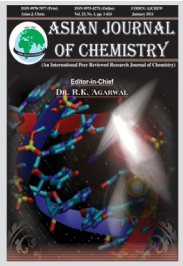
Asian Journal of Chemistry; Vol. 23, No. 4 (2011), 1628-1630

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in



Samarium Triflate Catalyzed Efficient Synthesis of Quinoxalines

P. RAGHUVEERACHARY and N. DEVANNA*

Department of Chemistry, Jawaharlal Nehru Technological University, Anantapur-515 002, India

*Corresponding author: E-mail: prvchari@gmail.com

(*Received*: 23 June 2010; *Accepted*: 7 December 2010) AJC-9374

A highly efficient method for the synthesis of quinoxalines derivatives has been developed using samarium triflate as catalyst. The method is applicable to a variety of 1,2-diketones and 1,2-diamines to afford the corresponding quinoxalines derivatives in high yields. All the reactions were carried out at acetonitrile reflux.

Key Words: Diketones, *ortho*-Phenylenediamines, Samarium triflate, Quinoxalines.

INTRODUCTION

Quinoxaline derivatives have received considerable interest from the pharmaceutical point of view because of their therapeutic activities such as antibacterial, antiviral, antiinflammatory, anticancer and kinase inhibitors. In addition, quinoxaline derivatives have been evaluated as antihelminthic agents, semiconductors, dyes and biocides[1-4]. Therefore, a variety of synthetic strategies have been developed for the preparation of substituted quinoxalines. Conventionally, quinoxalines synthesis can be achieved by the reaction of *o*-phenylene diamine with two-carbon synthones such as α-dicarbonyls, α-halocarbonyls, α-hydroxycarbonyls, α-azocarbonyls, epoxides and α,β-dihydroxy compounds[5-9]. Among the reported procedures, the most common method is the condensation of an aryl 1,2-diamine with 1,2-diketones in refluxing ethanol or acetic acid[10-12] or using different catalysts[13-16] and reaction conditions[17-20]. However, many of these methods suffer from several drawbacks, such as drastic reaction conditions, use of polar solvents, expensive and toxic metal catalysts, tedious work up procedures and unsatisfactory yields. Therefore, the development of simple and improved method for the synthesis of quinoxalines derivatives would certainly be useful in generating combinatorial libraries for drug discovery. In this work, a novel method is reported for the synthesis of quinoxalines derivatives *via* the coupling of aryl 1,2-diamines and 1,2-diketo compounds using a catalytic amount of samarium triflate under mild reaction conditions.

EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer FT-IR 240-C spectrophotometer using KBr optics. ^{1}H NMR spectra were recorded on Gemini-200 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV.

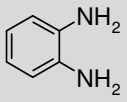
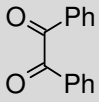
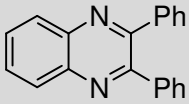
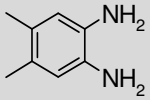
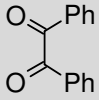
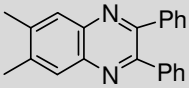
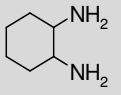
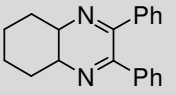
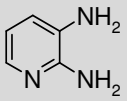
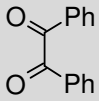
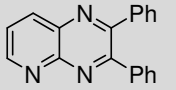
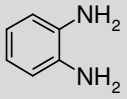
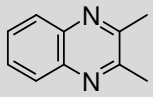
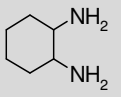
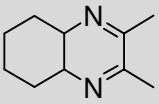
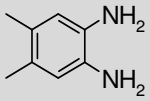
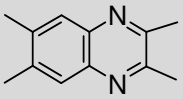
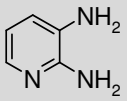
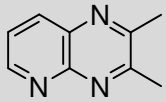
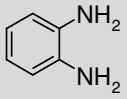
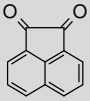
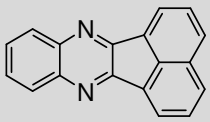
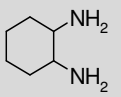
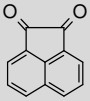
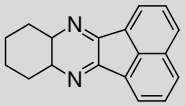
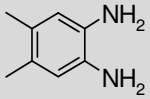
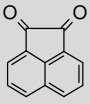
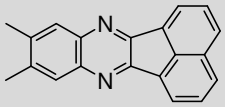
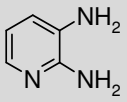
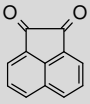
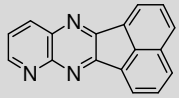
General procedure: To a mixture of diketone (1 mmol) and diamine (1 mmol) in acetonitrile (5 mL) was added the catalyst samarium triflate (10 mol %) at room temperature. The resulting reaction mixture was stirred at reflux for a period of specified period (Table-1). The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, as indicated by thin layer chromatography, the solvent was removed under reduced pressure. The residue was extracted with ethyl acetate (2 × 10 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to afford the crude products, which were purified by column chromatography using silica gel (60-120 mesh). All the products were confirmed by their ^{1}H NMR, IR and mass spectroscopic data.

Spectral data for selected compounds

Compound 3c: IR (KBr, ν_{max}, cm^{-1}): 3386, 2937, 2856, 1661, 1595, 1552, 1488, 1443, 1316, 1288, 1262, 1212, 1174, 1089, 1056, 979, 916, 850, 793, 766, 741, 695; ^{1}H NMR ($CDCl_3$): δ 1.35-1.45 (m, 3H), 1.50-1.62 (m, 2H), 1.85-1.95 (m, 1H), 2.50 (d, 1H, *J* = 6.0 Hz), 2.80 (d, 1H, *J* = 3.0 Hz), 7.15-7.28 (m, 6H), 7.32-7.42 (m, 4H). EIMS m/z (%): 289 (m^{+1} 100), 288 (10), 241 (10), 171 (10), 165 (15), 151 (10), 104 (60), 102 (30), 79 (25), 67 (35), 54 (10).

Compound 3d: IR (KBr, ν_{max}, cm^{-1}): 3413, 3058, 2923, 2853, 1592, 1549, 1433, 1385, 1338, 1242, 1189, 1123, 1070, 1020, 973, 922, 806, 776, 740, 698; ^{1}H NMR ($CDCl_3$): δ 7.25-7.40 (m, 6H), 7.45-7.55 (m, 2H), 7.58-7.63 (m, 2H), 7.75 (q, 1H, *J* = 6.5 Hz), 8.50 (dd, 1H, *J* = 3.5,10.0 Hz), 9.12-9.20 (m,

TABLE-1
SAMARIUM TRIFLATE CATALYZED SYNTHESIS OF QUINOXALINES

Entry	1,2-Diamine	1,2-Diketone	Product*	Reaction time (h)	Yield** (%)
a				5.0	90
b				4.5	92
c				6.0	84
d				5.0	85
e				5.0	85
f				7.0	72
g				5.0	88
h				5.0	78
i				4.5	89
j				6.0	80
k				4.5	90
l				5.0	85

*All the products were identified by their ^{1}H NMR, IR and mass spectral data; **Yields were isolated and unoptimized.

1H).; EIMS m/z (%): 284 (m^{+1} 100), 281 (12), 270 (15), 242 (20), 223 (10), 205 (10), 189 (15), 179 (35), 159 (20), 145 (20), 117 (30), 103 (40), 82 (56), 77 (10), 51 (10).

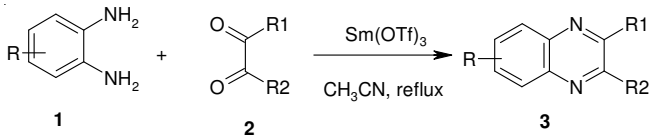
Compound 3g: IR (KBr, ν_{max}, cm^{-1}): 3383, 2940, 2850, 1620, 1563, 1494, 1442, 1399, 1367, 1325, 1255, 1200, 1158, 1113, 1095, 1044, 988, 907, 833, 769, 677; ^{1}H NMR ($CDCl_3$): δ 7.68-7.72 (m, 1H), 7.82-7.90 (m, 2H), 8.12-8.18 (m, 2H), 8.40 (d, 1H, *J* = 6.0 Hz), 8.01-8.10 (m, 2H), 9.12 (s, 1H). EIMS m/z (%): 255 (m^+ 25), 233 (56), 225 (18), 211 (33), 194 (15), 178 (30), 171 (65), 149 (20), 131 (25), 115 (15), 105 (100), 75 (28).

Compound 3h: IR (KBr, ν_{max}, cm^{-1}): 3376, 2994, 2947, 1641, 1599, 1560, 1461, 1395, 1313, 1238, 1191, 1151, 1108, 1041, 995, 918, 830, 796, 713, 680; ^{1}H NMR ($CDCl_3$): δ 2.78 (s, 3H), 2.83 (s, 3H), 7.58-7.68 (m, 1H), 8.35 (d, 1H, *J* = 5.0 Hz), 9.05 (d, 1H, *J* = 3.0 Hz). EIMS m/z (%): 159 (m^+ 48), 144 (10), 118 (58), 105 (12), 91 (15), 77 (52), 61 (100), 50 (18), 41 (66).

Compound 3i: IR (KBr, ν_{max}, cm^{-1}): 3387, 3064, 2938, 1661, 1592, 1449, 1323, 1211, 1172, 1110, 1045, 996, 927, 874, 794, 719, 681, 641; ^{1}H NMR ($CDCl_3$): δ 1.48-1.62 (m, 3H), 1.90-2.05 (m, 3H), 2.55 (d, 2H, *J* = 6.0 Hz), 3.08-3.18 (m, 2H), 7.68 (t, 2H, *J* = 6.0 Hz), 7.95 (d, 4H, *J* = 6.0 Hz).

RESULTS AND DISCUSSION

In a typical reaction, an equimolar amounts of *o*-phenylene diamine (**1**) with 1,2-diketo compound (**2**) were reacted in presence of samarium triflate (10 mol %) in acetonitrile at reflux condition to afforded the corresponding product of 2,3-diphenyl quinoxaline (**3a**) (Table-1, entry a). The reaction was completed within 5.0 h and the product was obtained in 90 % yield. The product was identified by its ^{1}H NMR, IR and mass spectroscopy. Subsequently, the reaction was extended to other substituted aryl 1,2-diamines and alicyclic 1,2-diamines (**1**) with a view to investigate the generality of the reaction for the synthesis of substituted quinoxalines (**3**) (**Scheme-I**) and the results were summarized in the Table-1.



1 2 3

Scheme-I

In present investigation, the condensation reaction of 4,5-dimethylbenzene-1,2-diamine with benzyl (entry b), biacetyl (entry g) and acenaphthylene-1,2-dione (entry k) were found to be superior in terms of reaction rate as well as in yields of the products. In other cases, the condensation reaction of cyclohexane-1,2-diamine with benzyl (entry c), biacetyl (entry f) and acenaphthylene-1,2-dione (entry j) were found to be comparatively slower than other reactants. In general, the condensation takes place faster, when the reaction was carried out between aromatic diamines and aromatic diketones. In a similar manner, the reaction between aliphatic diketones and alicyclic diamines was comparatively slower. All the reactions were carried out using the catalyst samarium triflate in 10 mol % only. In all the cases, the reactions were completed within 4.5 to 7.0 h of reaction time and the reactions were carried out at the reaction temperature of 80-85 ºC. In general all the reactions were very clean and the isolation of products also easy which were obtained in the range of 72-92 %. The structures of the products were identified by their ^{1}H NMR, IR and mass spectral analysis.

In conclusion, we have demonstrated a simple and efficient protocol for the synthesis of quinoxaline derivatives using a catalytic amount of samarium triflate at acetonotrile reflux *via* the coupling of diketo carbonyls with 1,2-diamines. The method is very simple, clean and applicable to a variety of reactants such as aromatic, hetero aromatic, aliphatic and alicyclic systems.

REFERENCES

1. F. Rong, S. Chow, S. Yan, G. Larson, Z. Hong and J. Wu, *Bioorg. Med. Chem. Lett.*, **17**, 1663 (2007).
2. J. Renault, M. Baron and P. Mailliet, *Eur. J. Med. Chem.*, **16**, 545 (1981).
3. S. Dailey, J.W. Feast, R.J. Peace, I.C. Sage, S. Till and E.L. Wood, *J. Mater. Chem.*, **11**, 2238 (2001).
4. X. Hui, J. Desrivot, C. Bories, P.M. Loiseau, X. Franck, R. Hocquemiller and B. Figadere, *Bioorg. Med. Chem. Lett.*, **16**, 815 (2006).
5. Z. Zhao, D.D. Wisnoski, S.E. Wolkenberg, W.H. Leister, Y. Wang and C.W. Lindsley, *Tetrahedron Lett.*, **45**, 4873 (2004).
6. B. Das, K.V. Lu, K. Suneel and A. Majhi, *Tetrahedron Lett.*, **48**, 5371 (2007).
7. J.S. Yadav, B.V.S. Reddy, Y.G. Rao and A.V. Narsaiah, *Chem. Lett.*, **37**, 348 (2008).
8. S. Antoniotti and E. Dunach, *Tetrahedron Lett.*, **43**, 3971 (2002).
9. C.S. Choa and S.G. Oh, *Tetrahedron Lett.*, **47**, 5633 (2006).
10. J.A. Kowalski, S.F. Leonard and G.E. Jr Lee, *J. Comb. Chem.*, **8**, 774 (2006).
11. K.M. Driller, S. Libnow, M. Hein, M. Harms, K. Wende, M. Lalk, D. Michalik, H. Reinke and P. Langer, *Org. Biomol. Chem.*, **6**, 4218 (2008).
12. M. Putala, N.K. Pustet and A. Mannschreck, *Tetrahedron Asym.*, **12**, 3333 (2001).
13. J.J. Cai, J.P. Zou, X.Q. Pan and W. Zhang, *Tetrahedron Lett.*, **49**, 7386 (2008).
14. C. Neochoritis, J.S. Stephanatou and C.A. Tsoleridis, *Synlett*, 302 (2009).
15. R.S. Bhosale, S.R. Sarda, S.S. Ardhapure, W.N. Jadhav, S.R. Bhusare and R.P. Pawar, *Tetrahedron Lett.*, **46**, 7183 (2005).
16. C. Srinivas, C.N.S.S.P. Kumar and V.J. Rao, *J. Mol. Catal. A*, **265**, 227 (2007).
17. C.S. Cho, W.X. Ren and S.C. Shim, *Tetrahedron Lett.*, **48**, 4665 (2007).
18. A. Staszewska, P. Stefanowicz and Z. Szewezuk, *Tetrahedron Lett.*, **46**, 5525 (2005).
19. J.F. Zhou, G.X. Gong, S.J. Zhi and X.L. Duan, *Synth. Commun.*, **39**, 3743 (2009).
20. S. Ajaikumar and A. Pandurangan, *Appl. Catal. A*, **357**, 184 (2009).