Asian Journal of Chemistry; Vol. 31, No. 10 (2019), 2211-2214

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2019.22110

One Pot Microwave Induced Synthesis, Characterization and Antibacterial Activity of Tetrazamacrocyclic Complexes of Transition Metal Ions of Bio-Inorganic Relevance

DEVENDRA KUMAR* and SARASWATI

Department of Chemistry, Institute of Basic Sciences, Dr. Bhimrao Ambedkar University, Khandari Campus, Agra-282002, India

*Corresponding author: E-mail: devendrakumar131@gmail.com

Received: 2 April 2019; *Accepted*: 3 May 2019; *Published online*: 30 August 2019; AJC-19524

Two new series of metal complexes, $[M(C_{18}H_{16}N_4O_4)\cdot 2H_2O]\ (CH_3COO^-)_2$ and $[M(C_{22}H_{24}N_4)\cdot 2H_2O]\ (CH_3COO^-)_2$, where M= $Co^{2+}/Ni^{2+}/Cu^{2+}$ have been prepared under microwave irradiation condition using microwave synthesizer. All the synthesized compounds were characterized by melting point determination of recrystallized samples, running single spot on TLC, elemental analyses, IR, UV-visible spectral studies. Synthesized macrocyclic complexes have been tested for their antibacterial activity against two bacteria *Klebsiella pneumoniae* and *Escherichia coli* by adopting disk diffusion method. The antibacterial activity was compared with amikacin antibiotic and it has been found that the complexes exhibited potential antibacterial activity. From the antibacterial studies, it has been found that the copper complexes were more effective on the microorganism in comparison to Ni(II) and Co(II) complexes.

Keywords: Transition metal(II) complexes, Tetrazamacrocyclic ligand, Infra-Red, UV-Visible, Antibacterial activity

INTRODUCTION

The population explosion and environmental pollution have created the attention of researchers in the discovery of new techniques for the wellbeing of mankind [1]. In recent decades, the greater part of the simple and cheap estimates that can be taken to diminish natural contamination and introduction to destructive synthetic concoctions have been executed. The better path is through the act of green science [2]. Due to eco-accommodating nature [3] microwave assisted synthesis are considered as a part of green science. Microwave assisted synthesis diminished contamination, offer exceptional returns and minimal effort together with effortlessness in preparing and handling [4]. Time required for the synthesis of macrocyclic complexes by microwave techniques have been accounted less as compare to regular methods [5]. In last two decades macrocyclic complexes are playing an extraordinary role in existing world view coordination chemistry due to their novel functionalities, structures, and properties [6]. Macrocyclic complexes have become very important due to their diversified applications such as catalyst [7], luminescent sensors [8] and control enzymes for cleaving DNA and RNA [9]. Copper complexes have been reported as DNA binding agents and for binding and activation of molecular oxygen [10]. Several macrocyclic complexes are used as dyes, pigments and as MRI contrasting agents [11,12]. In biological systems some metal porphyrins and derivatives of these porphyrins are used for transport and storage of oxygen in animals (*e.g.* haemoglobin and myoglobin) [13]. The macrocycles are used as antibiotic such as rifamycin (inhibits DNA polymerase) have remained in the centre of interest of biochemical chemists [14]. In analytical chemistry the transport capacity of the synthetic crown ethers has been reported because of their selective complexation with a variety of cation [15]. Manganese complex for the cyclam ligand show antimalarial activity [16] while Mn(II) macrocyclic complexes exhibited the antimicrobial activity [17]. Macrocyclic complexes of some transition metal ions showed anticancer activity [18,19]. Macrocyclic complexes of Eu(III) showed redox properties [20]. In recent years, researchers paying interest towards the synthesis of macrocyclic complexes of transition metal ions of bioinorganic relevance, containing variety of functional groups such as amide, oxamide, azomethine linkage [21-23]. In continuation of previous work [24,25], this article deals the microwave induced synthesis, characterization and

biological activity of macrocyclic complexes of Co(II), Ni(II) and Cu(II) ions by adopting the template reaction of acetylacetone/diethyl malonate with *o*-phenylenediamine.

EXPERIMENTAL

AR grade chemicals and solvent were used for synthesis of macrocyclic complexes. Metal salts were purchased from E. Merck. The macrocyclic complexes were synthesized by one pot template synthesis in order to produce high yield.

Synthesis of [5,7,12,14-Me$_4$-2,3,9,10-BzO$_2$[14]-1,4,8,11-N$_4$-2,4,7,9,11,14-hexene][M(II)] complexes (1a-c): *o*-Phenylenediamine (0.54 g, 0.005M) was dissolved in 15 mL ethanol and taken into a 100 mL round bottom flask. Then, cobalt (II) acetate tetrahydrate (0.62 g, 0.0025M) was dissolved in 15 mL distilled water. Metal salt solution was added dropwise with continuous stirring and mixture was irradiated in microwave synthesizer at 110 W, 68 ºC for 3 min. Thereafter, 15 mL ethanolic solution of acetylacetone (0.51 mL, 0.005 M) was mixed and again irradiated in microwave synthesizer at 110 W, 68 ºC for 5 min and allowed to cool. The obtained dark brown precipitate was filtered, washed with water followed by ethanol and dried a vacuum desiccator over anhydrous $CaCl_2$. Similarly, metal complexes of Ni(II) and Cu(II) were synthesized by using respective metal salts at 120 W, 70 ºC and 125 W, 75 ºC, respectively.

Synthesis of [2,4,9,11-tetraoxo-6,7,13,14 BzO$_2$[14]-1,5,8,12-tetraaza-6,13-diene][M(II)] complexes (2a-c): *o*-Phenylenediamine (0.54 g, 0.005 M) was dissolved in 15 mL ethanol and taken into a 100 mL round bottom flask. To this, cobalt(II) acetate tetrahydrate (0.62g, 0.0025 M), dissolved in 15 mL distilled water was added dropwise with continuous stirring. The mixture was irradiated in a microwave synthesizer at 115 W, 80 ºC for 3 min. After that, 15 mL ethanolic solution of diethyl malonate (0.76ml, 0.005 M) was mixed and again irradiated at 120 W, 80 ºC for 5 min and allowed to cool. A dark brown precipitate was obtained which was filtered, washed with water then by ethanol and dried over anhydrous $CaCl_2$ in a vacuum desiccator. In the similar manner, metal complexes of Ni(II) and Cu(II) were synthesized by using respective metal salts at 120 W, 78 ºC and 120 W, 80 ºC, respectively.

Antibacterial studies: Antibacterial activity of the synthesized compounds were screened against the bacteria *Klebsiella pneumoniae* and *Escherichia coli* (Gram -ve) by adopting disk diffusion method [26] in suitable nutrient medium MacConkey Agar purchased from market. The culture media was sterilized by moist heat sterilization method in an autoclave at 120 ºC at 15 pounds pressure for about 30 min then the sterilized culture media was spread homogeneously on petri-dish and allowed to solidify. The culture media was spread with prepared microbial log phase with the sterilized cotton bud. This process was conducted in sterilized laminar flow. 6 mm sterilized discs were carefully transferred at different places of culture plates. Solution of different concentrations 50, 25, 12.5, 6.25, 3.12 µg/mL of all the metal(II) complexes were prepared. All the metal(II) complexes were dissolved in 10 % methanol separately. From the above concentration 20 µL of each solution was pipette out and transferred on the sterilized discs. The petri dish were kept for incubation in an incubator at 37 ºC for 24 h.

RESULTS AND DISCUSSION

The purity of synthesized macrocyclic complexes was checked by calculating the repeated melting point in open capillaries and by running their TLC for single spot on silica gel-G plates. The synthesized complexes were soluble in CH_3OH, DMSO and DMF. Carbon, hydrogen and nitrogen analyses (Table-1) were carried out by using elemental analyser Euro-Vector. The IR spectra were recorded in the range of 4000-400 cm^{-1} on Bruker Spectrophotometer by using KBr pellets. The UV-visible spectra of the macrocyclic complexes were recorded on UV-VIS-NIR spectrophotometer Cary 5E in DMF/DMSO.

IR spectral studies: The complexes showed medium sharp intensity bands in the region 3149.96-3031.36 and 1450.13-1420.24 cm^{-1} may be due to C-H and C=C stretching vibrations of aromatic ring [27], respectively. IR spectra of macrocyclic complexes **1a-c** exhibited an absorption band in the region 2949.17-2917.26 cm^{-1} which may be due to C-H stretching vibrations [28] of CH_3 group. All macrocyclic complexes exhibited two bands in the region 3454.35-3321.86 and 934.61-820.67 cm^{-1} which indicate the presence of coordinating water molecules in the macrocyclic complexes [29].

Macrocyclic complexes **2a-c** exhibited an absorption band in the region 1694.46-1675.88 cm^{-1} which may be appeared due to stretching vibrations of >C=O. Macrocyclic complexes **2a-c** exhibited an absorption band in the region 3295.11-3217.62 cm^{-1} appeared due to N-H stretching vibrations. This value is lower than normal value which indicated the coordi-

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF MACROCYCLIC COMPLEXES **1a-c** AND **2a-c**

Compd. No.	Compounds	m.f.	m.w.	Colour	Elemental analysis (%): Calcd. (Found)			m.p. (°C)
					C	H	N	
1a	AA-OPDA Co(II)	$[Co(C_{22}H_{24}N_4)\cdot 2H_2O](CH_3COO^-)_2$	556.93	Dark brown	56.02 (56.92)	6.10 (7.06)	10.05 (11.07)	250 ± 2
1b	AA-OPDA Ni(II)	$[Ni(C_{22}H_{24}N_4)\cdot 2H_2O](CH_3COO^-)_2$	556.69	Black	56.04 (57.01)	6.10 (7.26)	10.05 (9.25)	200 ± 2
1c	AA-OPDA Cu(II)	$[Cu(C_{22}H_{24}N_4)\cdot 2H_2O](CH_3COO^-)_2$	561.54	Black	55.56 (56.43)	6.05 (5.38)	9.97 (10.65)	310 ± 2
2a	DEM-OPDA Co(II)	$[Co(C_{18}H_{16}N_4O_4)\cdot 2H_2O](CH_3COO^-)_2$	564.93	Dark brown	46.73 (47.38)	4.60 (5.62)	9.91 (10.86)	310 ± 2
2b	DEM-OPDA Ni(II)	$[Ni(C_{18}H_{16}N_4O_4)\cdot 2H_2O](CH_3COO^-)_2$	564.69	Dark brown	46.75 (47.66)	4.60 (5.38)	9.91 (9.05)	300 ± 2
2c	DEM-OPDA Cu(II)	$[Cu(C_{18}H_{16}N_4O_4)\cdot 2H_2O](CH_3COO^-)_2$	569.54	Black	46.35 (45.39)	4.56 (5.97)	9.83 (10.71)	320 ± 2

nation of N-H moiety with metal ion. IR absorption band in the complexes **1a-c** in the region 1599.61-1565.72 cm^{-1} may be appeared due to >C=N- stretching vibrations [30] of azomethine linkage. This region is lower region as compare to normal region *i.e*. 1620-1600 cm^{-1} which indicated that N-atom of azomethine linkage has participated in the coordination. All complexes exhibited a sharp intensity band in the region 1278.01-1211.93 cm^{-1} which may be due to C-N stretching vibrations. The appearance of new band in the IR spectra of all macrocyclic complexes in the region 510.33-492.86 cm^{-1} is probably due to the formation of M-N stretching vibrations [29] of newly formed M-N band.

Electronic spectral studies: The UV-visible spectra of Co^{2+} complexes [31] displayed three bands in the region 514.01-555.00, 662.03-672.04, 770.00-778.03 nm corresponding to transitions $^4T_{1g} \rightarrow {}^4T_{1g}$ (P), $^4T_{1g} \rightarrow {}^4A_{2g}$ (F) and $^4T_{1g} \rightarrow {}^4T_{2g}$ (F), respectively which suggested octahedral geometry for these complexes.

The UV-visible spectra of Ni(II) complexes [32] exhibited three bands in the region, 426.00-545.02, 554.02-699.01, 773.04-790.01 nm corresponding to transitions $^3A_{2g} \rightarrow {}^3T_{1g}$ (P), $^3A_{2g} \rightarrow {}^3T_{1g}$ (F) and $^3A_{2g} \rightarrow {}^3T_{2g}$ indicating octahedral geometry.

The UV-visible spectra of Cu(II) complexes [33] exhibited three bands in the region, 385.00-482.02, 612.03-627.04, 775.01-794.03 nm corresponding to transitions, $^2B_{1g} \rightarrow {}^2A_{1g}$, $^2B_{1g} \rightarrow {}^2B_{2g}$ and $^2B_{1g} \rightarrow {}^2E_{1g}$. These bands indicating distorted octahedral geometry for these complexes.

Elemental analyses, IR and electronic spectral data have suggested the probable structures (Fig. 1) of macrocyclic complexes.

Antibacterial activities: All the synthesized complexes were dissolved in five different concentrations (50, 25, 12.5, 6.25, 3.12 µg/mL) at each concentration different zone of inhibitions were obtained. Co(AA-OPDA) macrocyclic complex (**1a**) exhibited the zones of inhibition between 13-6 mm and 21-7 mm at different concentrations 50, 25, 12.5, 6.25, 3.12 µg/mL against *Klebsiella pneumoniae* and *Escherichia coli*, respectively. Similarly, Cu(AA-OPDA) macrocyclic complex (**1b**) exhibited the zones of inhibition between 21-7 and 22-9 mm at different concentrations against *Klebsiella pneumoniae* and *Escherichia coli*, respectively. Ni(AA-OPDA) macrocyclic complex (**1c**) also exhibited the zones of inhibition between 22-7 and 25-8 mm at different concentrations against *Klebsiella pneumoniae* and *Escherichia coli*, respectively.

Similarly, Co(DEM-OPDA) (**2a**) macrocyclic complex exhibited the zones of inhibition between 20-6 and 21-7 mm at different concentrations against *Klebsiella pneumoniae* and *Escherichia coli*, respectively. Cu(DEM-OPDA) macrocyclic complex (**2b**) exhibited the zones of inhibition between 21-7 and 22-8 mm at different concentrations *Klebsiella pneumoniae* and *Escherichia coli*, respectively. The Ni(DEM-OPDA) macrocyclic complex (**2c**) exhibited the zones of inhibition between 20-6 and 21-7 mm at different concentrations 50, 25, 12.5, 6.25, 3.12 µg/mL against *Klebsiella pneumoniae* and *Escherichia coli*, respectively. Among all the metal complexes the maximum

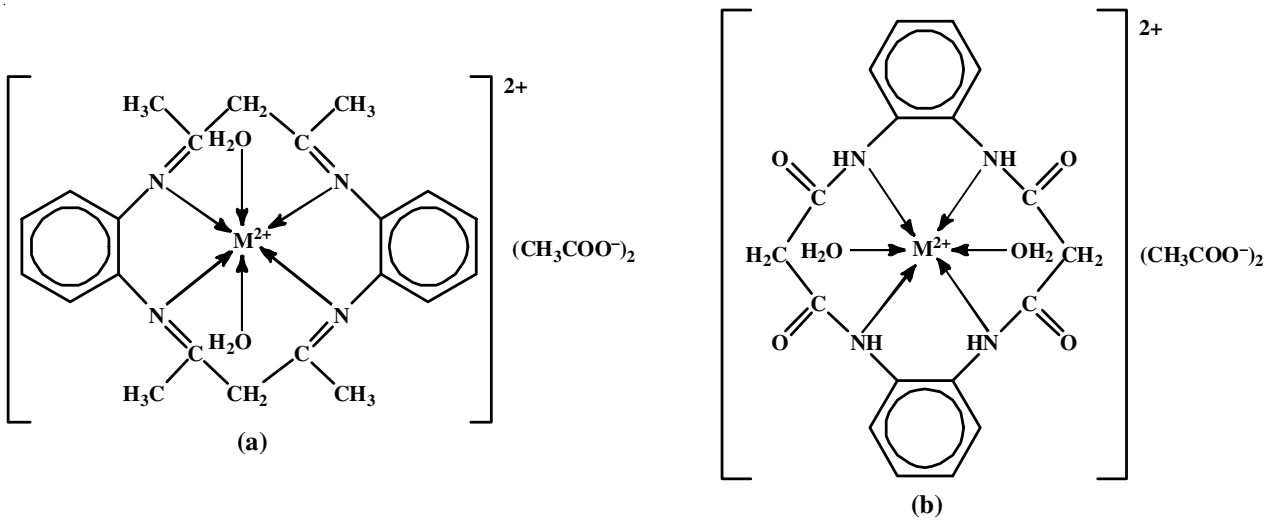

Fig. 1. Tentative structures of AA-OPDA (a) and DEM-OPDA (b) macrocyclic complexes (M^{2+} = Co^{2+}, Ni^{2+}, Cu^{2+})

TABLE-2
MAXIMUM ZONE OF INHIBITION (mm) FOR [M(AA-OPDA)] AND [M(DEM-OPDA)] COMPLEXES AGAINST TESTED MICROORGANISMS

S. No.	Conc. (µg/mL)	Co(AA-OPDA)		Ni(AA-OPDA)		Cu(AA-OPDA)		Co(DEM-OPDA)		Ni(DEM-OPDA)		Cu(DEM-OPDA)	
		EC	KP	EC	KP	EC	KP	EC	KP	EC	KP	EC	KP
1	50.0	21	13	25	22	22	21	21	20	21	20	22	21
2	25.0	14	12	18	20	18	16	18	17	19	16	20	19
3	12.5	10	9	15	16	16	14	17	15	18	15	18	16
4	6.25	9	8	12	14	13	12	13	12	12	10	14	12
5	3.12	7	6	8	7	9	7	7	6	7	6	8	7
Amikacin	3.12	12	8	12	8	12	8	12	8	12	8	12	8

EC = *Escherichia coli*, KP = *Klebsiella pneumoniae*

zone of inhibitions at least conc. 3.12 µg/mL was found 7 mm against *Klebsiella pneumoniae* and 9 mm against *Escherichia coli* for Cu(II) complexes. However, the zone of inhibition was less than the control amikacin which indicated that complexes are less active than standard drug amikacin (Table-2).

ACKNOWLEDGEMENTS

The authors are thankful to Dayalbagh Educational Institute, Agra, India for UV-visible spectral analysis, DST-FIST for providing fund for purchasing IR spectroscopy, SAIF, CDRI for elemental analyses and Ajay Diagnostic Centre, Jay Hospital and Research Pvt. Ltd. Agra, India for providing the facilities to screen antibacterial activity of the complexes.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. Shahid-ul-Islam, M. Shahid and F. Mohammad, *Ind. Eng. Chem. Res.*, **52**, 5245 (2013); https://doi.org/10.1021/ie303627x.
2. S.E. Manahan, Chemistry, Green Chemistry and Environmental Chemistry, In: Green Chemistry and the Ten Commandments of Sustainability, ChemChar Research Inc.: USA edn 2 (2006).
3. M. Hedidi, S.M. Hamdi, T. Mazari, B. Boutemeur, C. Rabia, F. Chemat and M. Hamdi, *Tetrahedron*, **62**, 5652 (2006); https://doi.org/10.1016/j.tet.2006.03.095.
4. K. Mahajan, M. Swami and R.V. Singh, *Russ. J. Coord. Chem.*, **35**, 179 (2009); https://doi.org/10.1134/S1070328409030038.
5. A.P. Mishra, N. Sharma and R.K. Jain, *Avan. Quím.*, **7**, 77 (2012).
6. J.K. Tang, Y.Z. Li, Q.L. Wang, E.Q. Gao, D.Z. Liao, Z.H. Jiang, S.P. Yan, P. Cheng, L.F. Wang and G.L. Wang, *Inorg. Chem.*, **41**, 2188 (2002); https://doi.org/10.1021/ic010674q.
7. J.H. Bi, M. Li and Y. Chen, *Asian J. Chem.*, **22**, 7389 (2010).
8. D. Parker, P.K. Senanayake and J.A. Gareth Williams, *J. Chem. Soc. Perkin II*, 2129 (1998); https://doi.org/10.1039/a801270i.
9. C.J. Burrows and J.G. Muller, *Chem. Rev.*, **98**, 1109 (1998); https://doi.org/10.1021/cr960421s.
10. J.G. Muller, X. Chen, A.C. Dadiz, S.E. Rokita and C.J. Burrows, *Pure Appl. Chem.*, **65**, 545 (1993); https://doi.org/10.1351/pac199365030545.
11. K.D. Karlin and Y. Gultneh, *Prog. Inorg. Chem.*, **35**, 219 (1987); https://doi.org/10.1002/9780470166369.ch3.
12. L.F. Lindoy, The Chemistry of Macrocyclic Ligand Complexes, Cambridge University Press: Cambridge, edn 2 (1989).
13. D.P. Singh, R. Kumar, V. Malik and P. Tyagi, *Transition Met. Chem.*, **32**, 1051 (2007); https://doi.org/10.1007/s11243-007-0279-2.
14. R. Huszánk, G. Lendvay and O. Horváth, *J. Bioinorg. Chem.*, **12**, 681 (2007).
15. D.W. Armstrong, K. Rundlett and G.L. Reid, *Anal. Chem.*, **66**, 1690 (1994); https://doi.org/10.1021/ac00082a015.
16. G.W. Gokel, W.M. Leevy and M.E. Weber, *Chem. Rev.*, **104**, 2723 (2004); https://doi.org/10.1021/cr020080k.
17. T.J. Hubin, P.N.A. Amoyaw, K.D. Roewe, N.C. Simpson, R.D. Maples, T.R.N. Carder Freeman, A.N. Cain, J.G. Le, S.J. Archibald, S.I. Khan, B.L. Tekwani and M.O.F. Khan, *Bioorg. Med. Chem.*, **22**, 3239 (2014); https://doi.org/10.1016/j.bmc.2014.05.003.
18. H.A. E1-Boraey and O.A. El-Gammal, *Open Chem. J.*, **5**, 51 (2018); https://doi.org/10.2174/1874842201805010051.
19. S. Ali, V. Singh, P. Jain and V. Tripathi, *J. Saudi Chem. Soc.*, **23**, 52 (2019); https://doi.org/10.1016/j.jscs.2018.04.005.
20. R.N. Pradhan, S.M. Hossain, A. Lakma, D.D. Stojkov, T.Z. Verbiæ, G. Angelovski, R. Pujales-Paradela, C. Platas-Iglesias and A.K. Singh, *Inorg. Chim. Acta*, **486**, 252 (2019); https://doi.org/10.1016/j.ica.2018.10.050.
21. A. Chaudhary and E. Rawat, *Int. J. Inorg. Chem.*, **2014**, Article ID 509151 (2014); https://doi.org/10.1155/2014/509151.
22. D.A. Robson, L.H. Rees, P. Mountford and M. Schroder, *Chem. Commun.*, **14**, 1269 (2000); https://doi.org/10.1039/b003019h.
23. L.A. Ehrlich, P.J. Skrdla, W.K. Jarrell, J.W. Sibert, N.R. Armstrong, S.S. Saavedra, A.G.M. Barrett and B.M. Hoffman, *Inorg. Chem.*, **39**, 3963 (2000); https://doi.org/10.1021/ic991033m.
24. S. Chaudhary and D. Kumar, *Proc. Nat. Acad. Sci. (India)*, **78**, 207 (2008).
25. D. Kumar and S. Singh, *J. Chem. Pharm. Res.*, **8**, 744 (2016).
26. K.R. Fiebelkorn, S.A. Crawford, M.L. McElmeel and J.H. Jorgensen, *J. Clin. Microbiol.*, **41**, 4740 (2003); https://doi.org/10.1128/JCM.41.10.4740-4744.2003.
27. D.P. Singh and V. Grover, *Acta Chim. Slov.*, **57**, 780 (2010).
28. S.N. Singh, R.K. Agarwal and M. Katyal, Molecular Structure: A Spectroscopic Approach, Discovery Publication: New Delhi (1990).
29. N.S. Gill, R.H. Nuttall, D.E. Scaife and D.W.A. Sharp, *J. Inorg. Nucl. Chem.*, **18**, 79 (1961); https://doi.org/10.1016/0022-1902(61)80372-2.
30. V.K. Sharma, O.P. Pandey, S.K. Sengupta and D.M. Halepoto, *Transition Met. Chem.*, **14**, 263 (1989); https://doi.org/10.1007/BF01098225.
31. A. Aukauloo, X. Ottenwaelder, R. Ruiz, S. Poussereau, Y. Pei, Y. Journaux, P. Fleurat, F. Volatron, B. Cervera and M.C. Muñoz, *Eur. J. Inorg. Chem.*, **7**, 1067 (1999); https://doi.org/10.1002/(SICI)1099-0682(199907)1999:7<1067::AID-EJIC1067>3.0.CO;2-7.
32. A.A. Hashmi, A.A. Sheikh, S. Shreaz and L.A. Khan, *J. Chem. Pharm. Res.*, **2**, 172 (2010).
33. R.A. Sheikh, S. Sheikh, L.A. Khan and A.A. Hashmi, *J. Chem. Pharm. Res.*, **2**, 274 (2010).