Heterocyclic Letters
Vol. 5 | No.3 | 329-334 | May-July| 2015
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

SYNTHESIS AND ANTIBACTERIAL ACTIVITY STUDIES OF 2, 3-DISUBSTITUTED QUINAZOLINONES-4(3*H*)-ONES

Glory Arava* and N.Venkatasubba Naidu*

Department of chemistry, Sri Venkateswarauniversity, Tirupati-517502, A.P, INDIA
E-mail: aglory999@gmail.com; nvsn69@gmail.com

Abstract:-We have demonstrated a one-pot synthesis of 2,3-disubstituted quinazolinones between o-azidobenzamides and benzyl alcohols via $FeCl_2$-DDQ catalysed dehydrogenations essentially under neutral conditions. All the synthesized compounds were fully characterized on the basis of their detailed spectral studies and the synthesized compounds were screened for their antibacterial activities strains using Cup plate method.

Keywords: $FeCl_2$-DDQ, antibacterial activity, Et_3N and DMAP in CH_2C1_2.

INTRODUCTION

Quinazolinone derivatives widely occur in natural products, and they show a wide range of useful biological and pharmacological activities. The quinazolinone derivatives exhibit many central nervous system (CNS) effects, such as analgesic, antiparkinsonian, CNS depressant, and CNS stimulant activities; they also act as psychotropic, hypnotic, cardiotonic, and antihistamine agents[IV,V] and possess cardiovascular activity (including antihypertensive, antiarrhymic, vasodilatory, and lipid-lowering effects) and antiinflammatory activity (including inhibition of cyclooxygenase activity and leukocyte function).[I,II] They are also potent antibacterial, antifungal, antiviral, antimycobacterial, and antimalarial agents and possess anthelmintic activity.[III] Quinazolinone derivatives are used as inhibitors of various enzymes, and these enzymes include monoamine oxidase, aldose reductase, tumor necrosis factor R, and thymidylate synthase.[III] Therefore, they are interesting as structural scaffolds and have been assigned as privileged structures in drug development.[IV]

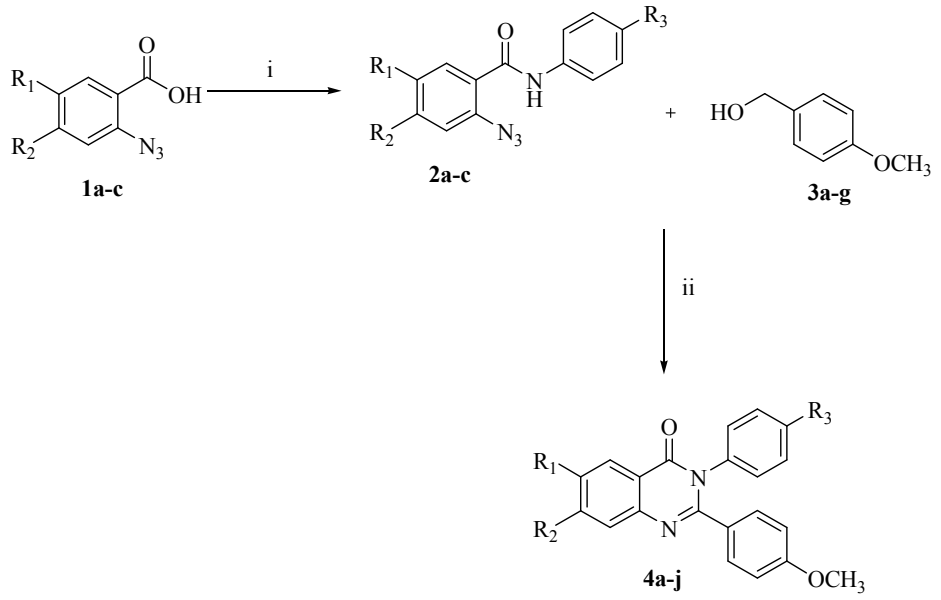
Triazole compounds contain three nitrogen atoms in the five-membered aromatic azole ring. They are readily able to bind with a variety of enzymes, and receptors in biological system via diverse non-covalent interactions, and thus display versatile biological activities [V-X]. The related researche in triazole-based derivatives as medicinal drugs have been an extremely active topic, and numerous excellent achievements have been acquired. Noticeably, a large number of triazole compounds as clinical drugs or candidates have been frequently employed for the treatment of various types of diseases, which have shown their large development value and wide potential as medicinal agents. Triazole compounds have an importance as medicinal drugs, including antifungal, anticancer, antibacterial, antitubercular, antiviral, anti-inflammatory and analgesic, anticonvulsant, antiparasitic, antidiabetic, anti-

obesitic, antihistaminic, anti-neuropathic, and antihypertensive as well as other biological activities [XI-XV].

RESULTS AND DISCUSSIONS

Condensation of 2-azidobenzoyl chloride and *p*-toluidine was carried out by using Et_3N and DMAP in CH_2C1_2 at 0 °C to 30 °C . afforded 2-azido-*N*-(*p*-tolyl)benzamide **2a** in 86% yield. Similarly, 2-azido-4,5-dimethoxy-N-(4- methoxyphenyl)benzamide **2b** was synthesized from the condensation of 2-azido-4,5-dimethoxybenzoyl chloride and *p*-anisidine by the same procedure. Likewise, the synthesis of 2-azido-*N*-(4- methoxyphenyl) benzamide **2c** was started from 2-amino benzoic acid **1a** and synthesized by the same procedure as described for compound **2a**. First, we heated a mixture of *o*-azidobenzamide (**2a**) and benzyl alcohol (**3a**) in the presence of $FeCl_2$ (10 mol %) and DDQ (1.25 equiv.) in CH_3CN at 70 °C for 2 h under N_2 atmosphere. To our delight, dehydrogenated product **4a** was obtained in 72% yield.

Figure1: synthetic scheme



Reagents and conditions: (i) (a) $SOC1_2$, reflux, 2 h (b) Et_3N, DMAP, CH_2C1_2, 0 °C to r.t,
(ii) o-azidobenzamide (1 mmol), 4-methoxybenzyl alcohol (1 mmol), solvent (5 mL)
2,3-dichloro-5, 6-dicyano-1, 4-benzoquinone (DDQ) (1.25 mmol).

Antibacterial Activity:

All the newly prepared compounds **(4a-j)** were screened for the antibacterial activity is done by the paper disc method [XVI, XVII]. Organisms used: Escherichia coli (Gram-negative) Staphylococcus aureus (gram-positive).

After solidification of media, petriplates inoculated with actively growing culture of Escherichia coli and Staphylococcus aureus separately as follows. Filter paper discs of 5 mm diameter were dipped in the test solution of different concentrations. After drying the disc, it was kept on Antibiotic med-3 agar in petriplates seeded with 1 ml bacterial culture of Escherichia coli and Staphylococcus aureus and incubated for 24 hrs at 37° C.

The antibacterial screening data showed that almost all the compounds **4a-j** are active and showing moderate to good antibacterial activity. Among the screened **4b**, **4e, 4f, 4j,** in

which respectively showed high activity against all the micro-organism employed. The activities of these compounds are almost equal to the standards the remaining compounds showed moderate to good antibacterial activity.

Table-1: Antibacterial activity

	Escherichia coli (Gram-negative) (Cone. µg/ml)			**Staphylococcus aureus** (gram-positive) (Cone. µg/ml)		
comp.	200	100	50	200	100	50
4a	22	21		12	21	9
4b	12	14	12	31	24	22
4c	11	13	8	-	14	7
4d	-	-	11	18	-	11
4e	18	19	30	28	19	23
4f	12	12	22	23	32	22
4g	23	19	17	11	19	17
4h	11	-	-	22	-	-
4i	22	11	17	13	11	17
4j	13	-	11	14	-	11

Experimental Section

General Conditions: All the used reactants, reagents and solvents were obtained from commercial sources and were of analytical grade. Melting points were determined by open capillary method. ^{1}H NMR (DMSO-d_6 300, 400 MHz) and ^{13}C NMR (DMSO-d_6, 75, 125 MHz) were recorded on spectrometer TMS as internal standard (chemical shifts and ppm). Mass spectra were recorded on a VG micromass70-70H instrument. The purity of the compounds was checked by TLC on silica gel plates using a mixture of n-hexane and ethyl acetate.

General procedure for the synthesis of quinazolin-4(3*H*)-ones (4a-j).

In an oven dried 10 mL round bottom flask, 2-azidobenzamide (0.162 g, 1 mmol) and *p*-hydroxy benzyl alcohol (0.124 g, 1 mmol) in dry CH_3CN (5 mL) were mixed and stirred at room temperature under N_2 atmosphere. To this, $FeCl_2$ (0.012 g, 10 mol %) and DDQ (0.283 g, 1.25 mmol) was added and reaction mixture was stirred at 70 °C for 2 h. The progress of reaction was monitored by TLC (using Petroleum Ether/AcOEt, 60:40 as an eluent). After completion of the reaction, reaction mixture was cooled down to room temperature and adsorbed on silica gel and crude was purified by column chromatography.

2-(4-methoxyphenyl)-3-(*P*-tolyl) quinazolin-4(3*H*)-one (4a).

m.p. 166-168 °C; IR (KBr): *V*max 3009, 2924, 2839, 1679, 1605, 1587, 1555, 1509, 1468, 1415, 1331, 1304, 1292, 1248, 1216, 1175, 1132, 1110, 1073, 1026, 953, 883, 831, 811 cm^{-1}; ^{1}H-NMR (500 MHz, CDC1$_3$): δ 2.33 (s, 3*H*, ArCH$_3$), 3.76 (s, 3*H*, ArOCH$_3$), 6.73 (d, 2*H*, *J* = 8.54 Hz, ArH), 7.03 (d, 2*H*, *J* = 8.24 Hz, ArH), 7.14 (d, 2*H*, *J* = 8.24 Hz, ArH), 7.30 (d, 2*H*, *J* = 8.54 Hz, ArH), 7.47-7.53 (m,, 1*H*, ArH), 7.77-7.81 (m, 2*H*, ArH), 8.33 (d, 1*H*, *J* = 7.62 Hz, ArH); ^{13}C-NMR (125 MHz, CDC1$_3$): δ 21.10, 55.16, 113.26, 120.69, 126.82, 127.08, 127.48, 127.89, 128.65, 129.59, 130.66, 134.48, 135.17, 138.13, 147.53, 154.99, 160.09, 162.46; ESI-MS: *m/z* 365 (M^++Na), 343 (M^++H); HRMS; calculated for $C_{22}H_{19}N_2O_2$ (M^++H) 343.1441 found,343.1442.

3-(*p*-tolyl)-2-(4-(trifluoromethyl)phenyl)quinazolin-4(3*H*)-one (4b).
m.p. 136-138 °C; IR (KBr): *V*max 1683, 1590, 1562, 1511, 1470, 1408, 1344, 1319, 1271, 1245, 1215, 1166, 1126, 1063, 1019, 953, 885, 841, 811, 770, 751, 691, 649, 603 cm^{-1}; ^{1}H-NMR (500 MHz, $CDC1_3$): δ 2.33 (s, 3*H*, $ArCH_3$), 7.03 (d, 2*H*, *J* = 8.39 Hz, ArH), 7,13 (d, 2*H*, *J* = 8.39 Hz, ArH), 7.47-7.52 (m,, 4*H*, ArH), 7.52-7.58 (m, 1*H*, ArH), 7.78-7.84 (m, 2*H*, ArH), 8.35 (d, 1*H*, *J* = 7.62 Hz, ArH); 13C-NMR (125 MHz, $CDC1_3$): δ 21.10, 120.97, 124.94, 127.21, 127.57, 127.70, 128.59, 129.40, 129.86, 130.88, 131.14, 134.42, 134.74, 138.80, 138.94, 147.18, 153.80, 162.04; ESI-MS: *m/z* 381 (M^++H); HRMS: calculated for $C_{22}H_{16}F_3N_2O$ (M^++H) 381.1209 found, 381.1213.

2-(4-nitrophenyl)-3-*O*-tolyl) quinazolin-4(3*H*)-one (4c).
m.p. 214-216 °C; IR (KBr): *V*max 3031, 2923, 2853, 1684, 1605, 1583, 1563, 1515, 1469, 1405, 1344, 1270, 1243, 1215, 1157, 1133, 1 108, 1073, 1018, 953, 887, 854, 810 cm^{-1}; ^{1}H-NMR (500 MHz, $CDC1_3$): δ 2.32 (s, 3*H*, $ArCH_3$), 7.03 (d, 2*H*, *J*= 8.39 Hz, ArH), 7.14 (d, 2*H*, *J* = 8.08 Hz, ArH), 7.51-7.61 (m,, 3*H*, ArH), 7.78-7.87 (m, 2*H*, ArH), 8.08 (d, 2*H*, *J* = 8.85 Hz, ArH), 8.36 (d, 1H, *J*= 7.93 Hz); ^{13}C-NMR (125 MHz, $CDC1_3$): δ 21.06, 120.93, 123.02, 127.15, 127.67, 127.77, 128.52, 129.91, 130.02, 134.16, 134.77, 138.99, 141.37, 146.93, 147.61, 152.96, 161.75; ESI-MS: *m/z* 380 (M^++Na), 358 (M^++H); ESI-MS: *m/z* 380 (M^++Na), 358 (M^++H); HRMS: calculated for $C_{21}H_{16}N_3O_3$(M^++H) 358.1186 found, 358.1188.

6,7-dimethoxy-2,3-bis(4-methoxyphenyl)quinazolin-4(3*H*)-one (4d).
m.p. 211-213 °C; IR (KBr): *V*max 3006, 2930, 2837, 1167, 1610, 1552, 1494, 1463, 1438, 1391, 1339, 1297, 1279, 1246, 1204, 1176, 1123, 1074, 1029, 1000, 958, 871, 835, 665 cm^{-1}; ^{1}H-NMR (500 MHz, $CDC1_3$): δ 3.76 (s, 3*H*, OCH_3), 3.79 (s, 3*H*, OCH_3), 4.01 (s, 3*H*, OCH_3), 4.02 (s, 3*H*, OCH_3), 6.73 (d, 2*H*, *J* = 8.85 Hz, ArH), 6.84 (d, 2*H*, *J* = 8.85 Hz, ArH), 7.06 (d, 2*H*, *J* = 8.85 Hz, ArH), 7.21 (s, 1*H*, ArH), 7.27 (d, 2*H*, *J* = 8.85 Hz, ArH), 7.64 (s, 1*H*, ArH); ^{13}C-NMR (125 MHz, $CDC1_3$): δ 55.19, 55.34, 56.28, 105.98, 107.99, 113.32, 113.98, 114.14, 128.07, 129.99, 130.57, 130.66, 143.79, 149.11, 154.10, 155.09, 158.97, 159.92, 161.98; ESI-MS: *m/z* 441 (M^++Na), 419 (M^++H); HRMS: calculated for $C_{24}H_{23}N_2O_5$ (M^++H) 419.1601 found, 419.1595.

6,7-dimethoxy-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)quinazolin-4(3*H*)-one (4e).
m.p. 216-218 °C; ^{1}H-NMR (500 MHz, $CDC1_3$): δ 3.71 (s, 6*H*, OCH_3), 3.79 (s, 6H, OCH_3), 4.02 (s, 3*H*, OCH_3), 4.03 (s, 3*H*, OCH_3),5.57 (s, 2H, ArH), 6.86 (d, 2*H*,*J* = 8.69 Hz, ArH), 7.09 (d, 2H, *J* = 8.69 Hz, ArH), 7.23 (s, 1*H*, ArH), 7.65 (s, 1*H*, ArH); ^{13}C-NMR (125 MHz, $CDC1_3$): δ 55.35, 55.94, 56.25, 60.75, 105.95, 106.73, 107.96, 114.08, 114.16, 129.75, 130.58, 138.58, 143.50, 149.26, 152.52, 153.77, 155.11, 159.11, 161.77; ESI-MS: *m/z* 479 (M^++H); HRMS: calculated for $C_{24}H_{23}N_2O_5$ (M^++H) 479.1812 found, 479.1803.

2-(2,4-dichlorophenyl)-3-(4-methoxyphenyl)quinazolin-4(3*H*)-one (4f).
m.p. 168-170 °C; IR (KBr): *V*max 3744, 3670, 3611, 3394, 3008, 2884, 2819, 2314, 1693, 1550, 1514, 1450, 1393, 1219, 772 cm^{-1}; ^{1}H-NMR (500 MHz, $CDC1_3$): δ 3.77 (s, 3*H*, OCH3), 6.74-6.87 (m, 2*H*, ArH), 6.92-7.01 (m, 1*H*, ArH), 7.18 (dd, 1*H*, *J*= 8.24 Hz, 1.37 Hz, ArH), 7.21-7.34 (m, 3*H*, ArH), 7.57 (t, 1*H*, *J* = 7.17 Hz, ArH), 7..76-7.87 (m, 2*H*, ArH), 7.37 (d, 1*H*, *J* = 7.78 Hz, ArH); ^{13}C-NMR (75 MHz, $CDC1_3$): δ 55.27, 114.21, 121.33, 126.84, 127.15, 127.64, 128.95, 129.40, 129.77, 130.95, 132.90, 133.39, 134.65, 135.67, 147.07, 152.32, 159.56, 162.04; ESI-MS: *m/z* 419 (M^++Na), 397 (M^++H); HRMS: calculated for $C_{21}H_{15}Cl_2N_2O_2$ (M^++H) 397.0510 found, 397.0512.

3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)quinazolin-4(3*H*)-one (4g).
m.p. 176-178 °C; IR (KBr): *V*max 3007, 2924, 2851, 1680, 1609, 1587, 1506, 1467, 1413, 1357, 1334, 1294, 1244, 1175, 1124, 1080, 1027, 1001, 897, 830, 752, 695, 663, 610 cm^{-1};

^{1}H-NMR (500 MHz, $CDC1_3$): δ 3.71 (s, 6H, OCH_3), 3.78 (s, 3H, OCH_3), 3.79 (s, 3*H*, OCH_3), 6.59 (s, 2*H*, ArH), 6.86 (d, 2*H*, *J* = 8.85 Hz, ArH), 7.09 (d, 2H, *J* = 8.85 Hz, ArH), 7.49-7.56 (m, 1*H*, ArH), 7.78-7.84 (m, 2*H*, ArH), 8.35 (d, 1*H*, *J* = 8.08 Hz ArH); ^{13}C-NMR (75 MHz, $CDC1_3$): δ 55.40,56.02,60.77, 106.94, 114.28, 120.85, 127.15, 127.58, 129.76, 130.48, 134.62, 138.89, 147.33, 152.63, 154.92, 159.23, 162.46; ESI-MS: *m/z* 441 (M^++Na), 419 (M^++H); HRMS: calculated for $C_{24}H_{23}N_2O_5$ (M^++H) 419.1601 found, 419.1596.

2,3-bis(4-methoxyphenyl)quinazolin-4(3*H*)-one (4h).

m.p. 17-173 °C; IR (KBr): *V*max 2924, 2850, 1650, 1619, 1585, 1506, 1468, 1415, 1357, 1334, 1294, 1244, 1175, 1124, 1080, 1027, 1001, 897, 610 cm^{-1}; ^{1}H-NMR (500 MHz, $CDC1_3$): δ 3.76 (s, 3*H*, OCH_3), 3.78 (s, 3*H*, OCH_3), 6.73 (d, 2*H*, *J* = 8.85 Hz, ArH), 6.84 (d, 2*H*, *J* = 8.85 Hz, ArH), 7.06 (d, 2*H*, *J* = 8.85 Hz, ArH), 7.30 (d, 2*H*, *J* = 8.85 Hz, ArH), 7.47-7.53 (m,, 1*H*, ArH), 7.77-7.82 (m, 2*H*, ArH), 8.33 (d, 1*H*, *J* = 7.74 Hz, ArH); ^{l3}C-NMR (125 MHz, $CDC1_3$): δ 55.17, 55.32, 113.31, 114.18, 120.67, 126.85, 127.09, 127.48, 127.86, 129.92, 130.44, 130.66, 134.52, 147.50, 155.15, 159.00, 160.07, 162.62; ESI-MS: *m/z* 359 (M^++H); HRMS: calculated for $C_{22}H_{19}O_3N_2$ (M^++H) 359.1390 found, 359.1395.

2-(2,4-dichlorophenyl)-3-(*p*-tolyl)quinazolin-4(3*H*)-one (4i).

m.p. 184-186 °C; IR (KBr): *V*max 2953, 2923, 2853, 1686, 1597, 1565, 1510, 1470, 1379, 1943, 1275, 1253, 1217, 1178, 1159, 1139, 1104, 1078, 1052, 1022, 953, 867, 813, 772, 696, 664 cm^{-1}; ^{1}H-NMR (300 MHz, $CDC1_3$): δ 2.30 (s, 3*H*, $ArCH_3$), 6.88-7.01 (m, 1*H*, ArH), 7.03-7.19 (m, 3*H*, ArH), 7.20-7.32 (m, 3*H*, ArH), 7.52-7.62 (m, 1*H*, ArH), 7.76-7.87 (m, 2*H*, ArH), 8.37.(d, 1*H*, *J* = 7.93 Hz, ArH); ^{13}C-NMR (125 MHz, $CDC1_3$): δ 21.13, 121.33, 126.80, 127.16, 127.49, 127.66, 128.43, 129.39, 129.57, 129.83, 130.97, 132.95, 133.28, 133.70, 134.70, 135.66, 139.02, 147.05, 152.10, 161.93; ESI-MS: *m/z* 381(M^++H); HRMS: calculated for $C_{21}H_{15}Cl_2N_2O$ (M^++H) 381.0556 found, 381.0562.

2-(benzo[d][l,3]dioxol-5-yl)-3-(*p*-tolyl)quinazolin-4(3*H*)-one (4j)

m.p. 169-170 °C; ^{1}H-NMR (500 MHz, $CDC1_3$): δ 2.34 (s, 3*H*, $ArCH_3$), 5.92 (s, 2*H*, -OCH_2O-), 6.63 (d, 1*H*, *J* = 8.08 Hz, ArH), 6.83 (dd, 1*H*, *J* = 8.08 Hz, 1.67 Hz, ArH), 6.88 (d, 1*H*, *J* = 1.67 Hz, ArH), 7.04 (d, 2*H*, *J* = 8.24 Hz, ArH), 7.15 (d, 2*H*, *J* =.'8.24 Hz, ArH), 7.48-7.54 (m,, 1*H*, ArH), 7.77-7.81 (m, 2*H*, ArH), 8.33 (d, 1*H*, *J* = 7.93 Hz, ArH); ^{13}C-NMR (125 MHz, $CDC1_3$): δ 21.13, 101.29, 107.78, 109.55, 120.79, 123.84, 127.00, 127.13, 127.52, 128.56, 129.29, 129.68, 134.56, 135.05, 138.26, 147.19, 147.37, 148.29, 154.70, 162.38; ESI-MS: *m/z* 379 (M^++Na), 357 (M^++H); HRMS: calculated for $C_{22}H_{17}N_2O_3$ (M^++H) 357.1233 found, 357.1237.

References

I. Sinha, S.; Srivastava, M. *Prog. Drug Res*., **1994**, 43, 143.

II. de Laszlo, S. E.; Quagliato, C. S.; Greenlee, W. J.; Patchett, A. A.; Chang, R. S. L.; Lotti, V. J.; Chen, T.B.; Scheck, S. A.; Faust, K. A.; Kivlighn, S. S.; Schorn, T. S.; Zingaro, G. J.; Siegl, P. K. S. *J. Med. Chem*., **1993**, 36, 3207.

III. Liverton, N. J.; Armstrong, D. J.; Claremon, D. A.; Remy, D. C.; Baldwin, J. J.; Lynch, R. J.; Zhang, G.; Gould, R. *J. Bioorg. Med. Chem. Lett*., **1998**, 8, 483.

IV. Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev*., **2003**, 103, 893.

V. (a) Viegas-Junior C, Danuello A, da Silva Bolzani V, et al. *Curr. Med. Chem*., **2007**,14(17), 1829-52. (b) Mehta G, Singh V. *Chem Soc Rev*., **2002**, 31, 324-34.

VI. Angel H. Romero,; Jose Salazar,; Simon E. Lopez, *Synthesis*, **2013**, 45, 2043-2050.

VII. (a) Kacker, I. K.; Zaheer. S. H.; *J. Indian. Chem. Soc*., **1951**, 28, 344. (b) Amin. A. H.; Mehta. D. R.; Samarth S. S.; *Prog. Drug. Res*., **1970**, 14, 218.

VIII. Buzas. A.; Hoffman. C. Bull. *Soc. Chim. Fr*. **1959**, 1889.

IX. Welch. W. M.; Ewing. F. E.; Huang. J; Menniti. F. S.; Pagnozzi. M. J.; Kelly. K.;

Seymour. P. A.; *Bioorg. Med. Chem. Lett*, **2001**, 177.

X. Gopalsamy, A.; Yang, H. *J. Comb. Chem*., **2000**, 2, 378.

XI. (a) Johne, S.; Groger, D. Pharmazie, 1970, 25, 22. (b) Coppola, M. *Synthesis*, **1980**, 505. (c) *Johne, S. Prog. Drug Res*., **1982**, 26, 259. (d) Johne, S. *Prog. Chem. Org. Nat. Prod*., **1984**, 46, 159. (e) Michael, J. P. *Nat. Prod. Rep.*, **2000**, 17, 603; and references cited therein.

XII. Koepfly, J. B.; Mead, J. F.; Brockman, J. A.*J Am.Chem.-Soc.*, **1947**, 69, 1837.

XIII. (a) Kacker, I. K.; Zaheer. S. H.; *J. Indian. Chem. Soc*., **1951**, 28, 344. (b) Amin. A. H.; Mehta. D. R.; Samarth S. S.; *Prog. Drug. Res*., **1970**, 14, 218.

XIV. Hughes, L. R. GB Patent 21883,19,**1987**.

XV. E. Pomarnacka,; M. Maruszak,; K. Langowska,; P. Reszka,; P.J. Bednarski. *Archpharm*. **2008**, 341,485-490 (Weinheim).

XVI. Barry AL. In The Antimicrobic Susceptibility Test: Principles and Practices; Lea and Febiger: Philadelphia; 1976; 45:180.

XVII. Reddy PM, Ho YP, Shanker K, Rohini R, Ravinder V. Physicochemical and biological
Characterization of novel macrocycles derived from *o*-phthalaldehyde. Eur. J. Med. Chem. 2009; 44:2621.

Received on 23 June, 2015.