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Synthesis and characterization of quinazolinobenzodiazepine-benzothiazole hybrid derivatives

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ABSTRACT

We have accomplished an efficient, convenient, and inexpensive and diversity oriented method for the synthesis ofbenzothiazole-quinazolinobenzodiazepine hybrid derivaties.The structures of all the newly synthesized molecules were assigned by elemental analysis and spectral data.

Keywords: Tetra butyl Ammonium Permanganate, Triethyl nitrate, THF: H_2O, MeCN.

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[45] and possess cardiovascular activity (including antihypertensive, antiarrhymic, vasodilatory, and lipid-lowering effects) and antiinflammatory activity (including inhibition of cyclooxygenase activity and leukocyte function).[1,2] They are also potent antibacterial, antifungal, antiviral, antimycobacterial, and antimalarial agents and possess anthelmintic activity.[3] Quinazolinone derivatives are used as inhibitors of various enzymes, and these enzymes include monoamine oxidase, aldose reductase, tumor necrosis factor R, and thymidylate synthase.[3] Therefore, they are interesting as structural scaffolds and have been assigned as privileged structures in drug development.[4]

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 [5-10]. 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 [11-15].

MATERIALS AND METHODS

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 ($CDCl_3$ 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 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 4-methyl-3-nitrobenzoic acid (2)
To a solution of 4-methylbenzoic acid (5 g, 36.76 mmol) in CH_2Cl_2, ammonium nitrate (2.94 g, 36.76 mmol) was added and stirred for 10-15 minutes. Then cone. H_2SO_4 (7.13 g, 3.89ml, 73.52 mmol,) was added slowly in adropwise manner to the reaction mixture at 0 °C over a period of 10-15 minutes with vigorous stirring. Stirring was continued at room temperature for a period of 4-5 hours till TLC showed the completion of the reaction. The reaction mixture was quenched with ice cold water (100 mL). The organic layer was separated and evaporated on rotaevaporater under reduced pressure, water was added to the resulting residue and filtered out the obtained solid and washed with water several times to remove any acidic impurities to give crude solid which on srecrystallization using EtOAc: petroleum ether afforded colorless prisms of **2** (5.85 g, 88%). m.p- 176-178 °C; ^{1}H-NMR (300 MHz, CDC1$_3$): δ 2.65 (s, 3H), 5.36 (bs, 1H), 7.41-7.49 (d, 1H, *J* =7.73 Hz), 8.08-8.16 (dd, lH, *J*= 1.55 Hz), 8.51-8.54 (d, 1H, 1.55 Hz).

N-(4-methoxyphenyl)-4-methyl-3-nitrobenzamide (3)
To a solution of p-anisidine (5 g, 40.65 mmol) in anhydrous THF (40 mL) at 0^{o}C under nitrogen atmosphere triethylamine (10.94 mL, 81.30 mmol) was added at 0^{o}C and stirred at the same temperature for 30 minutes. To this reaction mixture was added 4-methyl-3-nitrobenzoyl chloride which was prepared from 4-methyl-3-nitrobenzoic acid (**2**; 8.82 g, 48.78 mmol) and $SOC1_2$ (11.86 mL, 126.6 mmol) at 80^{o}C for 2 h, in THF (5 mL) at 0^{o}C. The mixture was stirred at the same temperature for 30 min and then at r.t. for 1 h. The solvent was evaporated and the resulting residue was dissolved in ethyl acetate (100 mL) and washed with water, brine solution and dried over Na_2SO_4, concentrated and recrystallized from methanol to get pale low solid **3** (9.88 g, 85%). m.p. 151-152^{o}C; IR (Neat): V*rnax* 3414, 3090, 2934, 2832, 1666, 1619, 1598, 1534, 1510, 1458, 1413, 1352, 1321, 1232, 1178, 1114, 1031, 837, 735 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.61 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 6.74-6.88 (d, 2H, *J* = 9.06 Hz, Ar-H), 7.44-7.54 (d, 1H, *J* = 8.12 Hz, Ar-H), 7.55-7.67 (d, 2H, *J* = 9.06 Hz, Ar-H), 8.11-8.21 (dd, 1H, *J* = 7.93 Hz, *J* = 1.70 Hz, Ar-H), 8.56-8.64 (m, 1H, Ar-H), 10.13 (bs, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ19.59, 54.72, 113.17, 121.94, 123.19, 131.22, 131.61, 132.26, 133.65, 135.58, 148.35, 155.60, 162.49; ESI-MS: *m/z* 287 (M^++H).

***N*-(4-methoxyphenyl)-4-methyl-3-nitrobenzothioamide (4)**
To a stirred solution of amide **3** (9.5 g, 33.21 mmol) in dry toluene (60 mL), Lawesson's reagent (8.05 g, 19.93 mmol) was added at 90^{o}C. The reaction mixture was refluxed for 2-3 hrs. After completion of the reaction (monitored by TLC) solvent was removed under reduced pressure. The resulting reaction mixture was quenched with 10 mL of Sodium hypochlorite aqueous solution on ice-cubes and filtered out the resulting solid to get dark yellow coloured crude product. Purification of the crude solid by column chromatography afforded pure pale yellow compound **4** (8.52 g, 85%). m.p. 133-135^{o}C; IR (KBr): *V*max 3447, 3147, 2971, 1612, 1560, 1529, 1447, 1348, 1307, 1251, 1163, 1107, 1074, 1030 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.57 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 6.92-7.10 (d, 2H, *J* = 9.07 Hz, Ar-H), 7.53-7.64 (d, 1H, *J* = 7.97), 7.67-7.79 (d, 2H, *J* = 9.07 Hz, Ar-H), 8.00-8.17 (dd, 1H, *J* = 9.07 Hz, J = 1.92 Hz), 8.35-8.51 (m, 1H), 11.87 (bs, 1H). ^{13}C-NMR (75 MHz,$CDCl_3$): δ 113.60, 123.20, 125.62, 131.70, 132.49, 132.66, 135.13, 140.87, 148.17, 157.40, 193.37; ESI-MS: m/z 303 (M^++H).

6-methoxy-2-(4-methyl-3-nitrophenyl)benzo[*d*]thiazole (5)
The *N*-(4-methoxyphenyl)-4-methyl-3-nitrobenzothioamide **4** (8 g, 26.49 mmol) was dissolved in a solution of NaOH (10.59 g, 264.9 mmol) in water (50 mL) and ethanol (5 mL). This mixture was added dropwise to a solution of potassium ferricyanide (34.86 g, 105.96 mmol) in water (50 mL) at 90^{o}C, stirred for 30 min, and then allowed to cool. The precipitate was collected, washed with water (2 x 100 mL) and purified by column chromatography to give pale yellow colored solid product **5** (6.99 g, 88%). m.p. 142-144^{o}C; IR (KBr): *V*max 3424, 2931, 2839, 1601, 1564, 1529, 1481, 1434, 1378, 1345, 1293, 1265, 1227, 1159.38, 1117.44, 1058.59, 1025.21, 985.94, 910.60, cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.62 (s, 3H), 3.86 (s, 3H), 7.00-7.11 (dd, 1H, *J* = 8.87 Hz, *J* = 2.26 Hz), 7.37-7.45 (d, 1H, *J* = 2.26 Hz), 7.46-7.55 (d, 1H, *J* = 7.93 Hz), 7.80-7.94 (d, 2H, *J* = 8.68 Hz), 8.05-8.16 (dd, 1H, *J* = 7.93 Hz,

J = 1.13 Hz), 8.49-8.58 (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.5, 55.8, 104.0, 116.2, 123.0, 124.0, 130.8, 132.9, 133.4, 135.4, 136.4, 148.4, 149.5, 158.1, 162.3. ESI-MS: m/z 301 (M^++H).

4-(6-methoxy-1,3-benzothiazole-2-yl)-2-nitrobenzoic acid (6)

Freshly prepared Ifetrabutylammonium Permanganate (12.63 g, 35.00 mmol) was added to a solution of 6-methoxy-2-(4-methyl-3-nitrophenyl)benzo[d]thiazole**5** (5 g, 16.66 mmol) in dry pyridine (30 mL) at room temperature. It was observed that the reaction was so exothermic, the reaction mixture started to reflux for 5-10 minutes even at room temperature. The reaction was continued to stirr at room temperature for a period of 12 hours. The completion of reaction was monitored by TLC. This reaction mixture was poured into a mixture of $NaHSO_3$ and cold dilutesHCl. Then, the reaction mixture was extracted with ethyl acetate (3x60 mL). The combined organic layers were removed by vacuum under reduced pressure to afford crude compound. Recrystallization using EtOAc : petroleum ether resulted into a free flowing light yellow colored solid **6** (5.06 g, 92%). m.p. 220-222^{o}C; IR (KBr): *V*max 3423, 2928, 2544, 1696, 1599, 1543, 1469, 1409, 1370, 1307, 1284, 1257, 1172, 1026 cm^{-1}; ^{1}H NMR (200 MHz, $CDC1_3$): δ3.91 (s, 3H), 7.06-7.15 (dd, 1H, *J* = 8.85 Hz, *J* = 2.72 Hz), 7.41-7.45 (m, 1H), 7.90-7.98 (m, 2H), 8.20-8.27 (d, 1H, *J* = 8.17 Hz), 8.42 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 55.79, 104.78, 116.80, 121.28, 124.04, 128.29, 130.59, 131.20, 136,26, 136.70, 147.70, 149.06, 158.11, 161.14, 165.27; ESI-MS: m/z 331 (M^++H).

(8))-Methyl 1-(4-(6-methoxybenzo[*d*] thiazo1-2-yl)-2-nitrobenzoyl) pyrrolidine-2-carboxy-late (8)

To a stirred suspension of 4-(6-methoxy-l,3-benzothiazole-2-yl)-2-nitrobenzoic acid **6** (5 g, 15.15 mmol) and thionyl chloride (7.20 g, 4.42 mL, 60.60 mmol) in dry benzene (50 mL) was added DMF (four-five drops) and the stirring was continued for 6 h. The benzene was evaporated in vacuum and the resultant oil **7** dissolved in dry THF (10 mL) and added drop wise over a period of 30 min to a stirred suspension of L-prolinemethylester hydrochloride (3.75 g, 22.72 mmol), triethylamine (4.59 g, 45.45 mmol) and THF : water (3:1, 50 mL) cooled in an ice bath. After completion of addition, the reaction mixture was brought to ambient temperature and stirred for an additional 2 h. The THF was evaporated in vacuum and the aqueous layer was diluted with water (50 mL) and extracted with ethyl acetate (3 x 50 mL) and washed with brine, dried over Na_2SO_4 and evaporated in vacuum and was purified by column chromatography to afford compound **8** (5.34 g, 80%). m.p. 149-150^{o}C; IR (KBr): *V*max 3008, 2954, 2881, 2837, 1741, 1639, 1601, 1558, 1535, 1482, 1428, 1345, 1320, 1262, 1219, 1173, 1092, 1059, 1024, cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ1.84-2.06 (m, 3H), 2.25-2.43 (m, 1H), 3.33-3.58 (m, 2H), 3.72 (s, 3H), 3.88 (s, 3H), 4.50-4.60 (m, 1H), 7.20 (dd, 1H, *J* = 9.06 Hz, 2.26 Hz), 7.71 (d, 1H, *J* = 7.93 Hz), 7.74-7.83 (m, 1H), 8.04 (d, 1H, *J*= 9.06 Hz), 8.47 (dd, 1H, *J* = 7.93 Hz, 1.51 Hz), 8.73 (d, 1H, *J* = 1.51 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 24.34, 28.97, 48.25, 51.86, 55.62, 58.13, 104.60, 116.51, 121.97, 123.82, 129.20, 132.43, 133.29,- 134.67, 136.37, 145.40, 147.61, 157.93, 161.07, 164.43, 171.59.

(S)-8-(6-methoxybenzo[*d*]thiazol-2-yl)-2,3-dihydro-1*H*-benzo[e]pyrrolo[l,2-a][l,4] diazepine-5,11(10*H*, 11a*H*)-dione (9)

Compound **8** (5 g, 11.33 mmol) was dissolved in methanol (40 mL) and added $SnCl_2.2H_2O$ (10.20 g, 45.35 mmol) was refluxed for 3 h or until the TLC indicated that reaction was complete. The methanol was evaporated under vacuum and the aqueous layer was then carefully adjusted to pH8 with 10% $NaHCO_3$ solution in ice water bath and then extracted with ethyl acetate (3x50 mL). The combined organic phase was dried over Na_2SO_4 and evaporated under vacuum to afford the dilactam**9** (3.43 g, 80%). m.p. decomposition at 220^{o}C, IR (KBr): *V*max 3744, 2920, 2850, 2314, 1796, 1737, 1627, 1596, 1549, 1486, 1458, 1325, 1219, 1061, 1036, 1005, cm^{-1}; ^{1}H-NMR (300 MHz,$CDCl_3$): δ 1.94-2.11 (m, 3H), 2.65-2.79 (m, 1H), 3.50-3.63 (m, 1H), 3.68-3.80 (m, 1H), 3.90 (s, 3H), 4.09 (d, 1H, *J* = 6.00 Hz), 7.08 (d, 1H, *J* = 8.00 Hz), 7.43 (s, 1H), 7.75-7.86 (m, 2H), 7.93 (dd, 2H, *J* = 8.00 Hz, 26.02 Hz), 10.55 (s, 1H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 23.0, 25.8, 47.0, 55.7, 56.2, 104.8, 116.4, 119.2, 121.8, 123.7, 127.9, 131.6, 136.0, 136.3, 137.1, 147.9, 157.8, 162.9, 163.9, 170.6; ESI-MS: m/z 402 (M^++Na), 380 (M^++H),349

(S)-10-(2-azidobenzoyl)-8-(6-methoxybenzo[*d*]nthiazol-2-yl)-2,3-dihydro-lH-benzo[e]pyrrrolo[1,2-α][1,4] diazepine-5,11(10*H*,11a*H*)-dione (10)

To a stirred solution of dione**9** (3 g, 7.91 mmol) in dry THF (30 mL) and DMSO (2 mL) was added triethylamine (1.59 g 15.83 mmol) under nitrogen atmosphere at 20^{o}C and stirred for 20 min. To this 4-dimethylamino pyridine (0.675 g, 5.54 mmol) was added in one portion and allowed to stirr at same temperature for 20 min. Then freshly prepared 2-azidobenzoyl chloride (1.57 g, 8.70 mmol) in dry THF (10 mL) was added dropwise over 10 min and stirred at 20^{o}C for 2 h. The solvent was evaporated under reduced pressure and the resulting residue was dissolved in dichloromethane (100 mL) and the organic layer was washed with water (2x30 mL), dried over anhydrous sodium

sulphate and evaporated to give the compound **10** (3.10 g) as thick liquid and used immediately in the next step without any further purification.

Synthesis of benzothiazole-quinazolinobenzodiazepine hybrid (11)

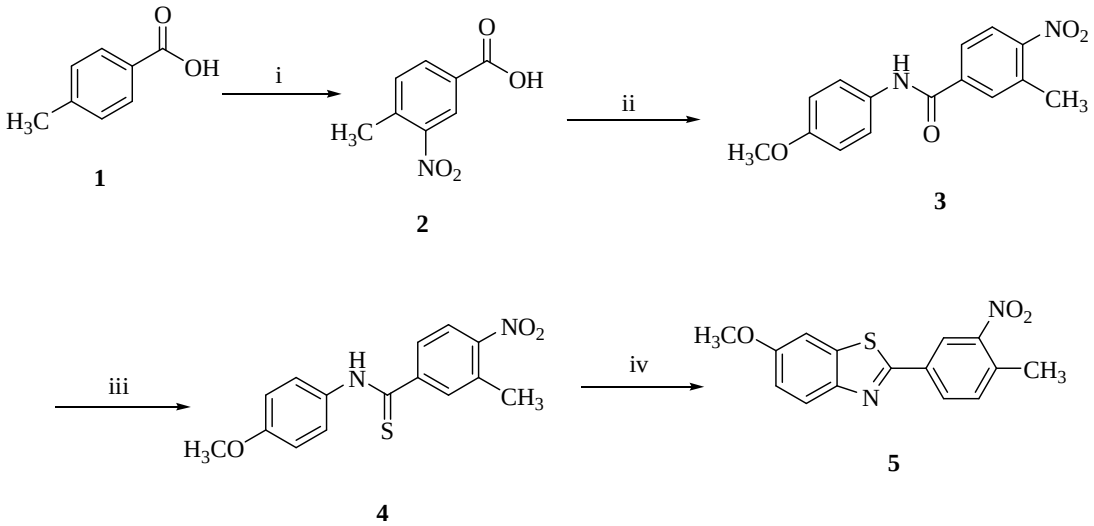
To a stirred solutionof azide intermediate **10** (3.1 g) in dry acetonitrile under nitrogen atm. was added 20 mole% $FeCl_2$ (0.149 g, 1.18 mmol) and 2,3-Dichloro-5,6-dicyano-l,4-benzoquinone (1.47 g, 6.50 mmol) at room temperature and reaction mixture was heated at 60^oC for 2 h. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure and the obtained residue was dissolved in DCM (100 mL) and washed with 10% NaOH solution (2 x 30 mL) and then with water and brine solution. Organic layer was dried over anhydrous sodium sulphate and evaporated under reduced pressure followed by purification by using column chromatography to give target compound benzothiazolequinazolinobenzodiazepine hybrid **11** as yellow solid (2.27 g, 60%). m.p. 199-202^oC; IR (KBr): *V*max 2955, 2923, 2853, 1691, 1644, 1600, 1557, 1514, 1464, 1431, 1362, 1296, 1263, 1219, 1181, 1126, 1079, 1061, 1025,-970 cm^{-1}; ^{1}H-NMR (300 ,MHz, $CDC1_3$): δ 1.98-2.45 (m, 3H), 3.14-3.29 (m, 1H), 3.56-3.72 (m/lH), 3.74-3.87 (m, 1H), 3.90 (s, 3H), 4.61 (d, 1H, *J* = 7.55 Hz), 7.11 (dd, 1H, *J*= 9.06 Hz, *J*= 2.26 Hz), 7.36 (d, 1H, *J* = 2.26 Hz), 7.51-7.61 (m, 1H), 7.74 (d, 1H, *J* = 7.55 Hz), 7.82 (td, 1H, *J* = 8.30 Hz, *J* = 1.51 Hz), 7.95 (d, 1H, *J* = 9.06 Hz), 8.09-8.16 (m, 2H), 8.30 (s, 1H), 8.36 (dd, 1H, *J* = 8.30 Hz, 1.51 Hz); ^{13}C-NMR (75 MHz, $CDC1_3$): δ 23.6, 27.0, 46.6, 55.7, 58.9, 104.0, 116.1, 121.4, 124.1, 127.0, 127.1, 127.5, 127.6, 127.8, 130.7, 133.5, 133.8, 134.8, 136.1, 136.7, 146.0, 148.5, 153.2, 158.1, 161.5, 162.8, 163.8; ESI-MS: m/z 503 (M^++Na), 481 (M^++H), 476, 545, 410, 396; HRMS: found: 481.1341 Calc.:481.1289; Elemental Analysis: found C, 67.48; H, 4.20; N, 11.66; O, 9.99; S, 6.67 Calc. C, 67.48; H, 4.20; N, 11.66; O, 9.99; S, 6.67.

RESULTS AND DISCUSSION

The nitration of *p*-toluic acid **1** by using NH_4NO_3 in the presence of concentrated H_2SO_4 in CH_2C1_2 at 0 °C to give white solid 4-methyl-3-nitrobenzoic acid **2** in 88% yield. Compound **2** was converted to its acid chloride by treating with thionyl chloride followed by condensation with the readily available *p*-anisidine in dry DCM by using triethyl amine afforded light brown crystals of amide **3** in 85% yield. The formation of amide **3** was confirmed by its ^{1}H NMR spectrum which showed two singlets of methyl and methoxy groups at δ 2.61 and δrespectively. It was further characterised with the characteristic amide NH appeared as a singlet at δ 10.13. Its ESI-MS peak appeared at 287 (M+H). The amide **3** was converted to its thioamide**4**, on treating with Lawesson's reagent in dry toluene under reflux condition to obtain thioamide**4** as pale yellow crystals in 8.5% yield. ^{1}H NMR spectrum of compound **4** showed characteristic thioamide NH singlet appeared in downfield region at δ 11.87.Intermolecular free-radical cyclization of thioamide**4** by using potassium -ferricyanide in aq. NaOH and ethanol at 100 °C for 2 h afforded compound **5** as a pale yellow solid in 88% yield. Product was evident from ^{1}H NMR spectrum which showed two singlets at δ 2.62 and δ 3.86 corresponding to aromatic CH_3 and OCH_3 respectively and one broad singlet in downfield region at δ 8.49-8.58 of aromatic proton adjacent to the nitro group.

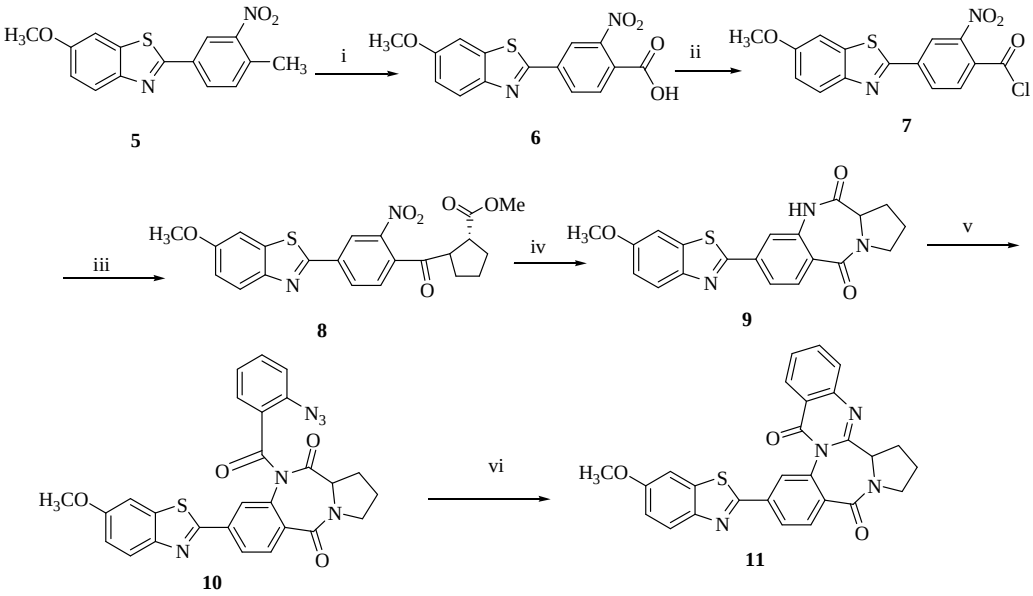
The compound **5** was oxidized with freshly prepared Tetrabutylammonium permanganate (TBAP) in dry pyridine at room temparature. afforded 4-(6-methoxybenzo[d]thiazol-2-yl)-2-nitrobenzoic acid **6** as a pale yellow solid in 92% yield. ^{1}H NMR spectrum of compound **6** showed a broad singlet at δ 3.25-3.8 corresponding to acidic proton, also the diappearance of singlet for methyl group at δ 2.62. Nitro acid **6** was converted to its acid chloride **7** with thionyl chloride in CH_2Cl_2, which was condensed with L-proline methyl ester in the presence of triethyl amine to obtain amide **8** in 80% yield as a brownish solid. ^{1}H NMR spectrum of compound **8** showed two singlets for OCH_3 group at δ 3.93 and δ 3.68. Its ESI-MS peak appeared at 442 (M+H). Amide **8** on reductive cyclisation by using $SnCl_2.2H_2O$ in methanol at reflux temperature afforded (S)-8-(6-methoxybenzo[d]thiazol-2-yl)-2,3-dihydro-lH-benzo[e]pyrrolo[l,2-a][l,4] diazepine-5,11(10H,11aH)-dione**9** in 75% yield as a faint yellow solid. It was confirmed from ^{1}HNMR spectrum by the appearance of a peak at δ 4.09 (d, 1H, *J* = 6.00 Hz) for chiral proton, and by the disappearance of a singlet of OCH_3 protons ofmethyl ester. Next step is the coupling of dilactam**9** with freshly prepared o-azido benzoyl chloride in dry THF:DMSO (3:1) by using Et_3N and DMAP at 20 °C for 2 h which gave azide intermediate **10** which was used in the next step immediately. Compound **10** was treated with $FeCl_2$ and DDQ in dry acetonitrile at 60 °C for 2 h afforded target compound circumdatin-benzothiazole hybrid **11** in 60% yield as a yellow colored solid. Product was confirmed from ^{1}H NMR spectrum which showed a doublet for chiral proton H-5 at δ 4.61 (d, 1H, *J* = 7.55 Hz) and one singlet appeared for aromatic OCH_3 protons at δ 3.90 (s, 3H).^{13}C NMR spectrum showed a peak at δ 58.9 for C-5, amides carbon C-10 showed a peak at δ 162.8 and C-16 showed peak at δ 161.5, quaternary imine carbon C-4 showed a peak at δ 153.2 and a peak observed at δ 55.7 for

aromatic OCH_3 carbon. Further it was cleared from ESI-MS which showed two peaks at 503 (M+Na) and at 481 (M+H).



Reagents and conditions: (i) NH_4NO_3, cone. H_2SO_4, CH_2C1_2, 0 °C-R.T., 4-5 h 88%
(ii) (a) $SOCl_2$, cat. DMF, CH_2Cl_2, 85% (b) P-Anisidine, Et_3N, THF, 0 °C-R.T.,85%
(iii) Lawesson's Reagent, toluene, 95 °C, 85% (iv) DMP, CH_2C1_2, R.T., 20 min., 88

Scheme-1



Reagents and conditions: (i) Tetra butyl Ammonium Permanganate (TBAP), dry Pyridine, 92%
(ii) $SOCl_2$, cat. DMF, CH_2C1_2, 97% (iii) L-proline methyl ester, Et_3N, THF:H_2O (3:1) 80%
(iv) $SnC1_2.2H_2O$, MeOH, reflux, 4h, 80%
(v) Et_3N, DMAP, THF, 20 °C, 2h (vi) $FeCl_2$, DDQ, MeCN, °C, 2 h, 60%.

Scheme-2

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