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Synthesis of 3 (N(1,3dioxo 1H benzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenylthiazolidine-4-carboxylic acid.

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ABSTRACT

Regioselective synthesis of 3(n(1,3dioxo1Hbenzo[de] isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenylthiazolidine -4-carboxylic acid were performed by coupling of 2-aryl-thiazolidin-4-caboxylic acids respectively with N-(ω-bromoalkyl)-1,8-naphthalimideusing K_2CO_3 in DMF medium. The structure of all the new compoundswere characterized by IR, ^{1}H-NMR, ^{13}C-NMR, and Mass spectral data.

Keywords: Terminal dibromoalkane; 1,8-naphthalimide;N-(ω-bromoalkyl)-1,8-naphthalimide;Coupling; Regioselective.

INTRODUCTION

With increasing demand to synthesis of Thiazolidine derivatives has an interesting biological activities, some of these are anticancer activity[1,2] , antioxidant[3,4] and also it has an interesting antimicrobial activity [5-8], in addition to it found in some literature has antidiabitic agents[9- 11].therefore they seemed desirable to synthesize some of 2-substituted-thiazolidine-4-carbonyl amino acid derivatives to try to improve it's antibacterial activity. As a part of our efforts to synthesis amino acids containing hetero cyclic compounds and studying their biological activities [12-14] and 2-aryl-thiazolidine-4-carboxylic acid amides as potent cytotoxic agents for both prostate cancer and melanoma [15-19], ATCAA was designed from lysophosphatidic acid (LPA) structure with a lipid chain in order to inhibit guanine-binding protein-coupled receptor (GPCR) signaling, which was involved in proliferation and survival of prostate cancer [20-23].The pharmacological importance thiazoles has prompted us to synthesize a series of novel3(n(1,3dioxo1Hbenzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenyl thiazolidine-4-carboxylic acid. The synthetic route were performed by coupling of 2-aryl-thiazolidin-4-caboxylic acids respectively with N-(ω-bromoalkyl)-1,8-naphthalimideusing K_2CO_3 in DMF medium.

MATERIALS AND METHODS

Materials and apparatus

Spectroscopic grade organic solvents were obtained from Finar chemicals. Starting and other chemicals and reagents were purchased from Sigma-Aldrich unless otherwise stated and were used without further purification. Thin layer chromatography (TLC) was performed on silica gel 60 F_{254}aluminum plates (Merck). The melting points reported were uncorrected and determined in Polmon instrument (model No. MP-96). The IR spectra were recorded on Bruker Infrared model Tensor-27. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker400 MHz Ultra shield spectrometer. The ESI mass spectra were recorded on a VG micro mass 7070-H.

Synthesis of 1H-benzo [de]isoquinoline-1,3(2H)-dione(2)

1,8-Naphthalic anhydride **(1)**(1g,5.07mmol) was taken in ammonia solution (60 mL) and stirred at 100^{o}C for 12 hours. After cooling, a yellowish solid is obtained, to this 200 mL of ice cold water is added and filtered at pump. The solid product was dried in oven at 100^{o}C and collect the compound.

General procedure for the synthesis of N-(ω-bromoalkyl)-1,8-naphthalimide(4a-f)
To a solution compound **(2)** (0.5gm, 1mmol) in acetonitrile (30 mL), anhydrous potassium carbonate (553 mg, 4 mmol) and terminal dibromoalkane (561 mg, 3mmol) were added and the mixture was refluxed for 12 h. After completion of the reaction, anhydrous potassium carbonate was removed by filtration and the solvent was evaporated under reduced pressure to get the crude product. This was further purified by column chromatography (10% EtOAc-hexane) to afford the compound.

General procedure for the synthesis of 2-aryl-thiazolidin-4-caboxylic acids(7_{1-2})
A mixture of L-cysteine (1.008g, 8.33mmol) and appropriate aldehyde (1g 8.3mmol) was taken in ethanol (150mL) and water (15mL) and stirred at room temperature for 12 h and collected the colourless solid 2-aryl-thiazolidin-4-caboxylic acid, washed with diethyl ether, and dried in the air, 2-Aryl-thiazolidin-4-caboxylic acids **(7_{1-2})** was collected.

General experimental procedure for the synthesis of 3(n(1,3dioxo1Hbenzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenylthiazolidine-4-carboxylic acid($8_{1-2\ a-f}$)
2-Aryl-thiazolidin-4-caboxylic acids**(7_{1-2})** (0.5g 2mmol) and N-(ω-bromoalkyl)-1,8-naphthalimide**($4_{\ a-f}$)** (0.62g 2mmol) and added anhydrous potassium carbonate (0.567g 4 mmol) were dissolved in 10 mL of DMF and the mixture was refluxed for 12 h. After completion of the reaction, anhydrous potassium carbonate was removed by filtration and DMF was removed in vacuo and poured into ice cold water stir with gloss rod and filtered the yellowish-orange colour pure compound**($8_{1-2\ a-f}$).**

Spectral Data
1H-benzo [de]isoquinoline-1,3(2H)-dione(2)
Yield 91.7%; Mp262-264^{o}C; IR (KBr) (cm^{-1}) 3440, 3059, 1701, 1676, 1622, 1586. ^{1}HNMR ($CDCl_3$, 400MHz) (δ) 7.79 (t, 2H), 8.45-8.43 (m, 4H), 11.71 (bs, 1H, D_2O exchanged). ESI-MS: *m/z* 198[M+H]$^{+}$.

2-(2-bromoethyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione(4 a)
Yield 87.8%; Mp 98-100^{o}C; IR (KBr) (cm^{-1}) 3088, 1688, 1659, 1586. ^{1}HNMR ($CDCl_3$, 400MHz) (δ) 2.37 (m 2H), 3.52 (t,J=6.8Hz 2H), 4.35 (t,J=7.2Hz 2H), 7.78 (t, J=7.2 Hz, 2H), 8.23 (d, J=8.4Hz, 2H), 8.61 (d, J=7.6Hz, 5H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ)28.52,39.85, 121.15, 125.93, 129.65, 130.91, 132.74, 133.85, 164.33.ESI-MS: m/z304 [M+H]$^{+}$.

2-(3-bromopropyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione(4 b)
Yield 89.6%; Mp 99-101^{o}C; IR (KBr) (cm^{-1}) 3098, 1697, 1676, 1598. ^{1}HNMR ($CDCl_3$, 400MHz) (δ) 2.37 (m 2H), 3.52 (t,J=6.8Hz 2H), 4.35 (t,J=7.2Hz 2H), 7.78 (t, J=7.2 Hz, 2H), 8.23 (d, J=8.4Hz, 2H), 8.61 (d, J=7.6Hz, 5H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ)29.89,34.92, 39.18, 121.33, 125.83, 129.10, 130.25, 131.44, 132.76, 164.12.ESI-MS: m/z318 [M+H]$^{+}$.

2-(4-bromobutyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione(4 c)
Yield 88.4%; Mp 100-103^{o}C; IR (KBr) (cm^{-1}) 3095, 1697, 1664, 1588. ^{1}HNMR ($CDCl_3$, 400MHz) (δ) 1.87-2.03 (m 4H), 3.47 (t, 2H), 4.23 (t, 2H), 7.75 (t, J=8 Hz, 2H), 8.21 (d,J=8.4 Hz, 2H), 8.60 (d, J=7.2 Hz, 5H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ) 26.89,30.25, 33.18, 39.34, 122.53, 126.93, 128.10, 131.25, 131.54, 133.96, 164.15. ESI-MS: m/z332 [M+H]$^{+}$.

2-(5-bromopentyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione(4 d)
Yield 87.2%; Mp118-120^{o}C; IR (KBr) (cm^{-1}) 3060, 2954, 1695, 1660, 1589, 1512. ^{1}HNMR ($CDCl_3$, 400MHz) (δ)1.58-1.63 (m, 2H),1.75-1.83 (m, 2H), 1.93-2.00 (m, 2H), 3.45 (t, *J* = 6.8Hz, 2H), 4.21 (t, *J* = 7.6Hz, 2H), 7.78 (t, *J* = 7.6Hz, 2H), 8.23 (d, *J* = 8.0Hz, 2H), 8.62(d, *J* =7.4Hz, 2H). ESI-MS: m/z: 346 [M+H]$^{+}$.

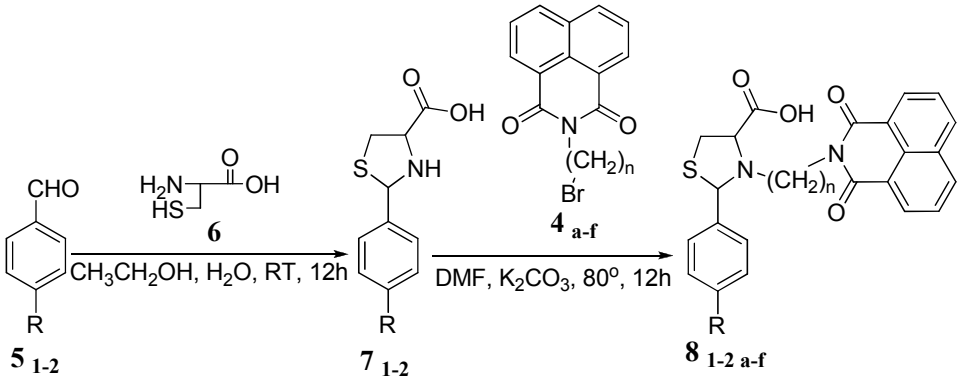
2-(6-bromohexyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione(4 e)
Yield 85.8%; Mp90-94^{o}C; IR (KBr) (cm^{-1}) 3061, 2954, 2932, 1694, 1662, 1587, 1512. ^{1}HNMR ($CDCl_3$, 400MHz) (δ)1.41-1.59 (m, 4H),1.69-1.79 (m, 2H), 1.84-1.93 (m, 2H), 3.37 (t, *J* = 6.79Hz, 2H), 4.14 (t, *J* = 7.6Hz, 2H), 7.73 (t, *J* = 7.93Hz, 2H), 8.16 (d,*J*= 8.03Hz, 2H), 8.55(d, *J* =7.36Hz, 2H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ) 26.39, 28.01, 32.87, 33.28, 40.33, 123.19, 126.92, 128.44, 131.10, 133.65, 164.14. ESI-MS: m/z360 [M+H]$^{+}$.

2-(8-bromooctyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione(4 f)
Yield 80.6%: Mp70-75^{o}C; IR (KBr) (cm^{-1}) 3061, 2934, 1697, 1661, 1588, 1510. ^{1}HNMR ($CDCl_3$, 400MHz) (δ) 1.30-1.44 (m, 8H),1.69-1.77 (m, 2H), 1.80-1.87 (m, 2H), 3.39 (t, *J* = 6.8 Hz, 2H), 4.17 (t, *J* = 7.6 Hz, 2H), 7.75 (t, *J* = 7.2Hz, 2H), 8.20 (d,*J*= 8.0 Hz, 2H), 8.59(d, *J* =7.2 Hz, 2H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ) 26.93, 28.01,

28.06, 28.55, 29.02, 32.77, 33.58, 40.34, 122.91, 126.82, 128.20, 131.02, 131.63, 133.61. 164.06. ESI-MS: m/z 374 $[M+H]^+$.

2-phenylthiazolidine-4-carboxylic acid(7_1)
Yield 98.7%; IR (KBr) (cm^{-1}) 3506, 3471, 2968, 2735, 2605, 2476, 2330, 1955, 1907, 1691, 1577, 1485, 1427, 1381, 1296, 1236, 1201, 1178, 1138, 1089; ^{1}HNMR (DMSO-d_6, 400MHz) (δ))3.14(m, 1H), 3.32(m, 1H), 3.49 (b s,1H), 4.19(t, J = 5.2Hz, 1H), 5.69 (s, 1H), 7.35 (t, J = 7.5Hz, 1H), 7.40 (t, J = 8.2Hz, 2H), 7.47 (d, J = 8.4Hz, 2H), 8.31 (s, 1H,), ESI-MS: *m/z* 210$[M+H]^+$.

2-(4-methoxyphenyl)thiazolidine-4-carboxylic acid(7_2)
Yield 98.5%; IR (KBr) (cm^{-1})3501, 3462, 2954, 2733, 2613, 2454, 2238, 1967, 1911, 1688, 1631, 1569, 1458, 1419, 1372, 1289, 1247, 1211, 1166, 1147, 1059;^{1}HNMR (DMSO-d_6, 400MHz) (δ))2.99(m, 1H), 3.12(m, 1H), 3.46 (s, 3H), 3.85 (b s,1H), 4.23(t, J = 5.24Hz, 1H), 5.86 (s, 1H),7.30 (d, J = 8.2Hz, 2H), 7.37 (d, J = 8.4Hz, 2H), 8.23 (s, 1H,),ESI-MS: *m/z* 240$[M+H]^+$.



R = H-1, R = OCH_3- 2,
n = a =2, b =3, c =4, d = 5, e = 6, f =8

Scheme 1: Synthesis of 3(n(1,3dioxo1Hbenzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenylthiazolidine-4-carboxylic acid($8_{1\text{-}6\ a\text{-}f}$)

3-(2-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)ethyl)-2-phenylthiazolidine-4-carboxylic acid($8_{1\ a}$)
MP 110-112^{0}C: IR (neat) (cm^{-1}) 34813374 ,3064 ,2957 ,2919 ,2850, 1696, 1653,1587,1513,1441,1408,1378,1347,1322,1260,1234,1072,1028. ^{1}H NMR (DMSO-d_6, 400MHz) (δ)2.52 (d, J = 2 Hz, 2H), 3.411 (s, 1H), 3.637 (t, J = 6.4Hz, 2H), 4.157 (t, J = 6.4 Hz, 2H), 4.843 (s, 1H), 7.851 (t, J = 8.4Hz, 3H), 8.306 (d, J =7.6 Hz, 2H). 8.442 (m, 6H), 11.738 (s, 1H).^{13}CNMR (DMSO-d_6, 400MHz) (δ)18.573, 25.682, 29.321, 60.788, 68.678, 101.540, 111.478, 112.847,113.410, 126.832, 127.931, 128.649, 153.848, 155.196, 160.636, 162.065, 162.217. ESI-MS: *m/z* 433$[M+H]^+$.

3-(3-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)propyl)-2-phenylthiazolidine-4-carboxylic acid($8_{1b)}$
MP 65-67^{0}C: IR (neat) (cm^{-1})3394, 2945, 2361, 1974, 1907, 1871, 1697, 1657, 1624, 1589, 1512, 1441, 1348, 1237, 1177, 1144, 1099, 1057, 1029. ^{1}H NMR (DMSO-d_6, 400MHz) (δ)1.82 (m, 2H), 2.33 (s, 1H), 2.51 (t, J = 2Hz, 2H), 2.731 (s,1H), 2.889 (s, 1H), 3.52 (t, J = 6.4Hz, 1H), 4.11 (t, J = 7.6Hz, 2H), 7.48(m,5H), 7.853(t, J = 8Hz, 2H), 8.42(d, J = 8.4Hz, 2H), 8.45(d, J = 7.2Hz, 2H), 10.014 (s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ)36.164, 41.008, 42.729, 48.533, 49.349, 64.231, 127.053, 132.250, 132.324, 132.652,133.418, 134.327, 134.417, 134.657, 135.751, 136.305, 139.324, 168.487 Mass (ES): *m/z*447 $[M+H]^+$.

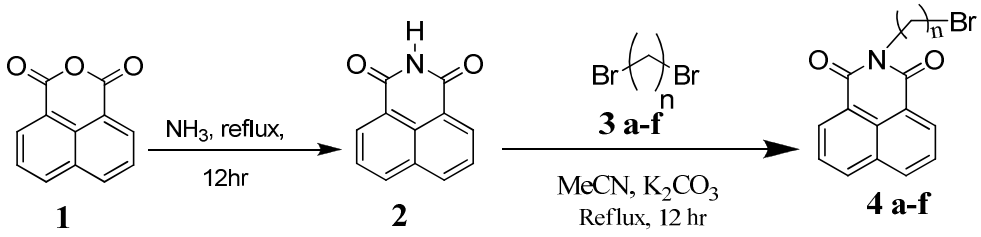
3-(4-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)butyl)-2-phenylthiazolidine-4-carboxylic acid(8_{1c})
MP 60-62^{0}C: IR (neat) (cm^{-1})3432,3014, 2952, 2877, 2630, 2406, 2360, 1949, 1879,1723,1616,1558,1511,1431,1390,1269,1203,1153,1071,1017. ^{1}H NMR (DMSO-d_6, 400MHz) (δ)1.574 (m, 2H), 1.779 (m, 2H), 2.37 (t, J = 8Hz, 2H), 2.514 (t, J = 1.6 Hz, 2H), 3.467 (t, J = 6.8Hz, 2H), 4.087 (t, J = 6.4Hz, 1H), 4.436 (s, 1H), 6.197 (m, 5H), 6.956(m, 2H), 7.648 (m, 4H), 10.027 (s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ)34.794, 41.626, 42.246,57.870, 58.253, 63.244, 122.515, 122.868,127.497, 127.575, 127.751, 130.399, 131.041, 131.638, 134.605, 134.760, 164.550, 163.929. ESI-MS: *m/z* 460$[M+H]^+$.

3-(5-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)pentyl)-2-phenylthiazolidine-4 carboxylic acid(8_{1d})
MP 70-72^{0}C: IR (neat) (cm^{-1})3497, 3018, 2942, 2864, 2745, 2601, 2455, 1962, 1911,1870,1654,1590,1513,1440,1346,1238,1144,1071,1030,. ^{1}HNMR(DMSO-d_6, 400MHz)(δ)1.365 (m, 2H), 1.476 (m, 2H), 1.636 (m, 2H), 2.52 (t, J = 1.6Hz, 2H), 2.742 (s, 1H), 2.902 (s, 1H). 3.401 (t, J = 6.4 Hz, 2H), 4.03 (t, J = 7.2Hz, 2H), 7.778 (m, 2H), 7.854 (t, J = 8Hz, 3H), 8.458 (m, 6H), 10.028 (s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz)

(*δ*)23.552, 25.650, 27.876, 28.684, 32.688, 38.120, 43.428, 60.965, 122.296, 122.408, 127.482, 127.583, 127.700, 130.990, 131.083, 131.669, 134.555, 134.655, 163.669, 163.750.ESI-MS: *m/z* 475[M+H]$^+$.

3-(6-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)hexyl)-2-phenylthiazolidine-4-carboxylic acid(8_{1e})
MP 72-74^{0}C: IR (neat) (cm^{-1}) 3414, 3064, 2936, 2861, 2361, 1713, 1658, 1623, 1590,1513,1440,1361,1224,1171,1142,1069,1030. ^{1}H NMR (DMSO-d_6, 400MHz) (*δ*)1.341 (m, 4H), 1.423 (m, 2H), 1.632 (m, 2H), 1.986 (s, 1H), 2.508 (m, 2H), 2.553(s, 1H), 3.373(t, *J* = 7.6Hz, 2H), 4.039(t, *J* = 7.2Hz, 1H), 4.36 (s, 1H), 7.451 (t, *J* = 7.6Hz, 4H), 7.524 (t, *J* = 7.2Hz, 1H), 7.873 (t, *J* = 8.4Hz, 2H), 8.488 (m, 4H), 9.211(s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz) (*δ*)25.702, 26.906, 27.848, 27.877, 28.012, 32.857, 44.703, 61.081, 63.654, 122.539, 127.701, 127.825, 127.906, 128.655, 129.014, 131.193, 131.668, 131.770, 131.992, 134.765, 163.859.ESI-MS: *m/z* 489[M+H]$^+$.

3-(8-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)octyl)-2-phenylthiazolidine-4-carboxylic acid(8_{1f})
MP 71-73^{0}C: IR (neat) (cm^{-1})3379, 2945, 2836, 2361, 2050, 1903, 1868, 1832,1698,1657,1590,1453,1235,1172,1112,1028. ^{1}H NMR (DMSO-d_6, 400MHz) (*δ*)1.271 (m, 8H), 1.606 (m, 2H), 1.96 (s, 2H), 2.516(m, 2H), 3.358 (s, 2H), 4.011(m, 2H), 4.138 (t, *J* = 4Hz, 1H), 4.324(s, 1H), 7.302 (m, 4H), 7.475 (m,1H), 7.864 (m,2H), 8.438 (m, 4H), 10.027 (s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz) (*δ*)30.618, 31.580, 31.673, 32.572, 32.631, 34.001, 37.629, 65.935, 84.287, 127.014, 127.111, 132.279, 132.382, 134.366, 134.684, 135.822, 135.911, 136.415, 139.470, 139.819, 168.568. ESI-MS: *m/z* 517[M+H]$^+$.



Where n = 2-a, 3-b, 4-c, 5-d, 6-e, 8-f.
Scheme 2: Synthesis of N-(ω-bromoalkyl)-1,8-naphthalimide(4 a-f)

3-(2-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)ethyl)-2(4methoxyphenyl)thiazolidine-4-carboxylic acid(8_{2a})
MP 98-100^{0}C: IR (neat) (cm^{-1})3433, 3009, 2931, 2868, 1674, 1600, 1510, 1438, 1410, 1387, 1317, 1259, 1218, 1180, 1163, 1095, 1062, 1028. ^{1}H NMR (DMSO-d_6, 400MHz) (*δ*)2.526 (t, *J* = 1.6Hz, 2H), 2.745(s, 2H), 2.905 (s,3H), 3.645 (t, *J* = 6.4Hz, 2H), 3.875(s, 1H), 4.16(t, *J* = 6.4Hz 1H), 7.139 (d, *J* = 8.8Hz 2H), 7.849 (t, *J* = 8 Hz, 4H), 8.451(m, 4H), 9.876 (s,1H). ^{13}CNMR (DMSO-d_6, 400MHz) (*δ*)31.201, 36.231, 42.226, 56.101, 58.257, 63.254, 114.888, 122.466, 127.519, 127.714, 130.355, 130.995, 131.609, 132.214, 134.561, 162.794, 163.895, 191.727.ESI-MS: *m/z* 463[M+H]$^+$.

3-(3-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)yl)propyl)2(4methoxyphenyl)thiazolidine-4-carboxylic acid(8_{2b})
MP 58-60^{0}C: IR (neat) (cm^{-1}) 3451, 3015, 2960, 2601, 2456, 2363, 1956, 1913, 1873,1656,1587,1513,1443,1348,1269,1234,1173,1120,1057,1026. ^{1}H NMR (DMSO-d_6, 400MHz) (*δ*)1.565(m, 2H), 1.725(t, *J* = 7.2Hz, 2H), 2.554(t, *J* = 5.6Hz, 2H), 3.469 (m, 4H), 3.961 (t, *J* = 6.8Hz, 2H), 4.338(s, 1H), 6.989(d, *J* = 8.8Hz 2H), 7.623 (t, *J* = 7.6Hz, 4H), 8.178(m, 4H), 9.765 (s,1H). ^{13}CNMR (DMSO-d_6, 400MHz) (*δ*)31.346**,** 34.699, 36.120, 37.895, 56.102, 58.433, 59.441, 114.765, 114.808, 121.985, 127.261,129.902, 129.933, 130.754, 131.303, 132.156, 134.366, 163.513, 191.601. ESI-MS: *m/z* 477[M+H]$^+$.

3-(4-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)butyl)-2(4methoxyphenyl)thiazolidine-4-carboxylic acid(8_{2c})
MP 78-80^{0}C: IR (neat) (cm^{-1}) 3376, 2944, 2834, 1698, 1658, 1592, 1512, 1443, 1388, 1348, 1252, 1178, 1029. ^{1}H NMR (DMSO-d_6, 400MHz) (*δ*)1.503(m,2H), 1.697(m,2H), 2.539 (t, *J* = 1.6Hz,2H), 3.064 (t, *J* = 4.4Hz, 2H), 3.457(m, 4H), 3.741(d, *J* = 4.4Hz 2H), 3.877(s, 1H), 7.136(d, *J* = 8.8Hz 2H), 7.834(t, *J* = 7.6Hz, 4H), 8.434(m, 4H), 9.882 (s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz) (*δ*)29.656, 24.829, 30.581, 56.116, 60.337, 60.957, 61.210, 114.883, 115.502, 122.291, 127.512, 130.034, 131.026, 131.586, 132.208, 134.607, 163.706, 164.615, 191.696. ESI-MS: *m/z* 491[M+H]$^+$.

3-(5-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)pentyl)2(4methoxyphenyl)thiazolidine-4-carboxylic acid(8_{2d})
MP 80-82^{0}C: IR (neat) (cm^{-1}) 3385, 2940, 2865, 2360, 1978, 1942, 1905, 1869, 1832, 1793, 1698, 1658, 1623, 1589, 1510, 1439, 1386, 1346, 1238, 1174, 1144, 1108, 1056, 1030. ^{1}H NMR (DMSO-d_6, 400MHz) (*δ*)1.362(m,2H), 1.472(m,2H), 1.638(m,2H), 2.511(s, 2H), 3.387 (m,4H), 3.809(s, 1H), 4.039(t, *J* = 7.2Hz 2H), 4.388(t, *J* = 4.4Hz 2H), 6.957(d, *J* = 2.4Hz 2H), 7.869(t, *J* = 7.6Hz, 4H), 8.479(m, 4H), 9.874 (s, 1H). ^{13}CNMR (DMSO-d_6,

400MHz)(δ)23.546, 25.629, 27.440, 27.899, 32.696, 60.955, 63.253, 67.556, 86.017, 122.547, 127.592, 127.701, 127.832, 129.671, 131.090, 131.199, 131.777, 134.767, 153.111, 163.867, 167.673.ESI-MS: *m/z* 505$[M+H]^+$.

3-(6-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)hexyl)-2(4methoxyphenyl)thiazolidine-4-carboxylic acid(8_{2e})
MP 80-82^{0}C: IR (neat) (cm^{-1}) 3383, 2935, 2860, 2454, 2052, 1964, 1906, 1871, 1657, 1512, 1462, 1348, 1248, 1177, 1031. ^{1}H NMR (DMSO-d_6, 400MHz) (δ)1.286 – 1.643(m,8H), 2.511(t, *J* = 2Hz, 2H), 2.991(s, 3H), 3.234(s, 1H), 3.379 (t, *J* = 2Hz, 2H), 3.82(d, *J* = 6Hz 2H), 4.057(t, *J* = 3.6Hz 1H), 7.146(d, *J* = 8.8Hz 2H), 7.875(t, *J* = 5.2Hz 4H), 8.489(m,4H), 9.876 (s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz)(δ) 26.831, 26.949, 30.218, 30.617, 33.330, 37.375, 37.550, 37.769, 55.145, 65.828, 127.175, 132.427, 132.462, 134.575, 134.861, 135.939, 136.463, 137.042, 139.510, 139.592, 168.590, 168.641.ESI-MS: *m/z* 519$[M+H]^+$.

3-(8-(1,3-dioxo-1H-benzo[de]isoqunolin-2(3H)-yl)octyl)-2(4methoxyphenyl)thiazolidine-4-carboxylic acid(8_{2f})
MP 88-90^{0}C: IR (neat) (cm^{-1}) 3494, 3350, 3017, 2931, 2857, 2458, 2361, 2226, 1964, 1908, 1869, 1698, 1659, 1590, 1512, 1440, 1387, 1350, 1239, 1174, 1139, 1075, 1032. ^{1}H NMR (DMSO-d_6, 400MHz) (δ)1.318(m,8H), 1.619(m,4H), 2.522(m, 4H), 2.657(t, *J* = 7.2Hz, 2H), 3.37 (t, *J* = 6.4Hz, 2H), 3.875(s,1H), 4.015(d, *J* = 7.2Hz 2H), 7.142(d, *J* = 8.4Hz 2H), 7.849(t, *J* = 8.4Hz 4H), 8.455(m,4H), 9.878 (s, 1H). ^{13}CNMR (DMSO-d_6, 400MHz) (δ)30.647, 31.587, 32.643, 32.777, 34.030, 37.684, 43.136, 49.057, 60.868, 65.920, 119.674, 120.299, 127.014, 127.104, 132.235, 132.330, 135.852, 136.397, 137.003, 139.417, 168.408, 168.502.ESI-MS: *m/z* 547$[M+H]^+$.

RESULTS AND DISCUSSION

The present investigation focuses on the development of a few3(n(1,3dioxo1Hbenzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenylthiazolidine-4-carboxylic acid(**$8_{1\text{-}2\ a\text{-}f}$**)were performed by the coupling of 2-aryl-thiazolidin-4-caboxylic acids(**$7_{1\text{-}2}$**) respectively with N-(ω-bromoalkyl)-1,8-naphthalimide**(4 $_{a\text{-}f}$)** using K_2CO_3 in DMF medium. The synthetic chemistry employed to prepare the target compounds is outlined in **scheme 1**.Regioselective synthesis of final compound involves threesteps: (1) Preparation of N-(ω-bromoalkyl)-1,8-naphthalimide**(scheme 2**),(2) Synthesis of 2-aryl-thiazolidin-4-caboxylic acids(**scheme 1**) and (3) couplingreaction of3(n(1,3dioxo1Hbenzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenyl thiazolidine-4-carboxylic acid with 2-aryl-thiazolidin-4-caboxylic acids andN-(ω-bromoalkyl)-1,8-naphthalimide(**scheme 1**).

CONCLUSION

Synthesis of few 3(n(1,3dioxo1Hbenzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenylthiazolidine-4-carboxylic acid reported. The structure of these new compounds was established by spectral studies. In this chapter I have successfully demonstrated a simple and convenient route for the synthesis of3(n(1,3dioxo1Hbenzo[de]isoquinolin-2(3H)-yl)alkyl)-2-(4-substituted) phenylthiazolidine-4-carboxylic acid reported by using the K_2CO_3 in DMF medium bycoupling of2-aryl-thiazolidin-4-caboxylic acids with N-(ω-bromoalkyl)-1,8-naphthalimide. In addition to its simplicity and mild reaction conditions, this method provides a wide range of new compound in good yield in a single step operation. These products are under investigation for their biological activities.

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