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Synthesis of novel isoindolone-based medium-sized macromolecules and triazole containing heterocyclic compounds

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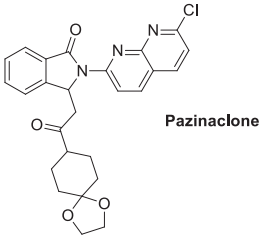
Abstract

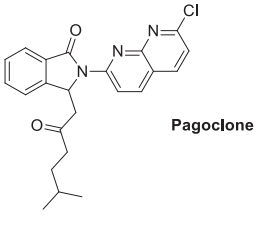
A series of novel isoindolone-based macromolecules of medium-sized heterocyclic rings, such as 7,8-dihydro-6*H*-benzo[4,5][1,6,3]dioxazonino[2,3-a]isoindol-14(9a*H*)-one derivatives (**5a-l**), were synthesized and its frame work incorporating with a triazole moiety on phenol, ie, 2-(4-((1-(2-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)isoindoline-1,3-dione (**9a-f**) and also a triazole moiety on carboxylic acid, ie, (1-(2-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl)benzoate derivatives (**13a-e**) with various substitutions on aryl ring system have synthesized. All the synthesized compounds were characterized and confirmed with IR, ^{1}H NMR, ^{13}C NMR, and ESI mass spectral analysis.

1 | INTRODUCTION

Indoline and isoindolines are the heterocyclic regio isomers, fused with benzene and saturated five membered rings. Isoindoline moiety is an important privilege ring system, because their derivatives are valuable backbones for the discovery of various new biologically active molecules including anxiolytic, psycotropic agents, hypnotics, anticonvulsants, antiepileptics,[1–4] and sedatives.[5,6] Pazinaclone is a sedative drug, which contains isoindoline as core moiety. It is used as anxiolytic at low doses and sedative at high doses. Isoindoline itself not used as a drug but its analogues, such as modification of functional groups, elongation or contraction chain or formation of macromolecules show some remarkable medicinal importance. Few marketed drugs, which are having isoindolin framework, are pazinaclone and pagoclone.



Pazinaclone



Pagoclone

In our present work, we report the synthesis of macromolecules containing medium-sized rings, such as 7,8-dihydro-6*H*-benzo[4,5][1,6,3]dioxazonino[2,3-a]isoindol-14(9a*H*)-one derivatives (**5a-l**) containing isoindoline ring and N-substituted isoindoline-1,3-dione compounds, such as 2-(4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)isoindoline-1,3-dione derivatives (**9a-f**) and (1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl)benzoate derivatives (**13a-e**).

2 | RESULTS AND DISCUSSIONS

The synthesis of 7,8-dihydro-6*H*-benzo[4,5][1,6,3]dioxazonino[2,3-a]isoindol-14(9aH)-ones (**5a-l**) were from commodity of chemicals, proceeds in multiple steps, in which insertion of 5-substituted 2-amino phenols (**2a-d**) in pthalic anhydride gave compounds **3a-d** and reduction of **3a-d** afforded compounds **4a-d** with reported procedures.[7,8] By analyzing the spectral data, we concluded that out of two carbonyl groups, one carbonyl acts as ketone, and other carbonyl acts as amide of compounds **3a-d**, and they were confirmed by FTIR and ^{1}H NMR spectroscopy. The confirmative peak at aliphatic region

as singlet due to benzylic hydrogen and further it was confirmed by FTIR spectroscopy. Repeated the same synthetic procedure to remaining all the compounds **4a-d** and finally compounds **4a-d** were cyclized with 1,3-dibromo propane and 1,4-dibromo butane and 1,5-dibromo pentane in the presence of sodium hydride afforded the desired medium-sized macromolecules **5a-l** with reported experimental procedure,[9] and complete physical data were presented in Table 1.

The Synthesis of 2-(4-((1-phenyl-1*H*-1,2,3-triazol-4-yl) methoxy)phenyl)isoindoline-1,3-dione derivatives (**9a-f**) were involved in three steps. Here, 4-amino phenol with pthalic anhydride in acetic acid at 100°C gave compound **7**, and propargylation of compound **7** afforded the corresponding 2-(4-(prop-2-yn-1-yloxy)phenyl)isoindoline-1,3-dione (**8**) in the presence of potassium carbonate and subsequently treated with various azides (which are generated from amines, diazotization followed by nucleophilic substitution) via 1,3-dipolar cyclo addition (click reaction) in the presence of 10 mol% of sodium ascorbate and 10 mol% of copper sulphate[10] afforded 2-(4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl) isoindoline-1,3-dione (**9a-f**) derivatives in excellent yields 70% to 81% as shown in scheme 2 and physical data presented in Table 2.

Synthesis of (1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl) benzoate (**13a-e**) were also involved 3 steps. i.e., insertion of 4-amino benzoic acid in pthalic anhydride followed by propargylation gave prop-2-yn-1-yl 4-(1,3-dioxoisoindolin-2-yl)benzoate **(12)** in presence of potassium carbonate and subsequently treated with various azides and 10 mol% of sodium ascorbate and 10 mol% of copper sulphate afforded the final compounds (**13a-e**) via 1, 3 dipolar cyclo addition (Click Reaction) and results were presented in Table 2.

TABLE 1 Physical data of compounds **5a-l**

Entry	Product	R	n	M Pt, °C	Yield[a], %
1	**5a**	H	1	68-70	69
2	**5b**	H	2	206-208	67
3	**5c**	H	3	188-190	61
4	**5d**	CH3	1	70-72	79
5	**5e**	CH3	2	152-154	76
6	**5f**	CH3	3	128-130	72
7	**5g**	Cl	1	96-98	62
8	**5h**	Cl	2	174-176	63
9	**5i**	Cl	3	170-172	59
10	**5j**	NO2	1	128-130	49
11	**5k**	NO2	2	150-152	45
12	**5l**	NO2	3	160-162	46

[a]Isolated yield.

TABLE 2 Physical data of compounds **9a-f** and **13a-e**

Entry	Product	M Pt, °C	Yield[a], %
1	**9a**	170-172	79
2	**9b**	183-185	81
3	**9c**	225-227	80
4	**9d**	260-262	73
5	**9e**	222-224	70
6	**9f**	193-195	74
7	**13a**	174-176	78
8	**13b**	162-164	62
9	**13c**	170-172	73
10	**13d**	164-166	61
11	**13e**	142-144	76

[a]Isolated yield.

3 | CONCLUSION

We have synthesized variety of molecules containing 2-phenylisoindolin-1-one as core moiety. Along with this core moiety, we have introduced a medium-sized rings ranging from 9 to 11 numbered in the final molecules, ie, 7,8-dihydro-6*H*-benzo[4,5][1,6,3]dioxazonino[2,3-a]isoindol-14(9a*H*)-one (**5a-l**) derivatives and also introduced a 1,2,3-triazole ring on the side chain of the phenyl ring of core moiety with different functional groups. Such as 2-(4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)isoindoline-1,3-dione derivatives (**9a-f**) and (1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl) benzoate derivatives (**13a-e**).

4 | EXPERIMENTAL

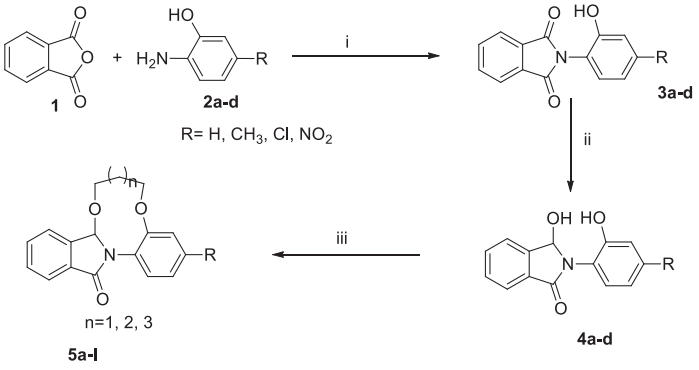
All the reagents and solvents are purchased from commercially available sources. Analytical TLC was performed on Merck Silica Gel GF254 plates, visualization by I_2 vapors/UV light. Melting points were recorded in open capillary tubes on SISCO electrical melting point apparatus and are uncorrected. IR spectra were obtained by using Perkin–Elmer spectrophotometer using potassium bromide optics. ^{1}H and ^{13}C NMR spectra recorded on a Bruker Avance 400 spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C) in $CDCl_3$/DMSO using TMS as an internal standard. ESI Mass Spectra recorded on Quatro LC Micromass (Waters Manchester, UK) mass Spectrometer.

4.1 | Typical procedure for the synthesis of 7,8-dihydro-6*H*-benzo[4,5][1,6,3] dioxazonino[2,3-a]isoindol-14(9a*H*)-one derivatives (5a-l)

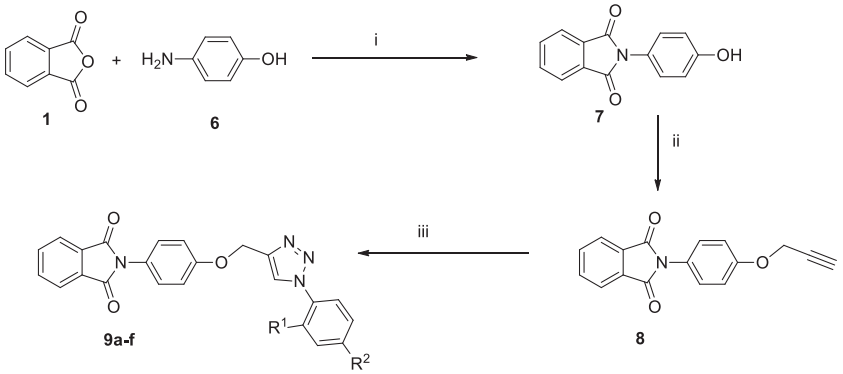
Synthesis of compounds (**5a-l**) (Scheme 1) involved in three steps. In the first step, to a stirred solution of pthalic anhydride (**1**, 2 g, 0.013 mol) and 2-amino phenol (**2a**, 1.47 g, 0.013 mol) in 20 ml of acetic acid and stirred at 100°C for 3 hours and poured the reaction mixture into crushed ice and filtered to afford the desired compound (**3a**) with 85% of yield. Second step, to a stirred solution of compound **3a** (0.8 g, 0.003 mol) in methanol (5 mL) was added sodium borohydride (0.08 g, 0.002 mol) at 0°C and stirred at RT for 2 hours to afforded compound **4a** with 90% of yield. Final step, to a stirred solution of compound **4a** (0.2 g, 0.008 mol) in 2 ml of DMF was added sodium hydride (0.384 g, 0.016 mol) at 0°C and stirred for 15 minutes. Then, added 1,3-dibromo propane (0.166 g, 0.008 mol) and stirred it RT for 2 hours to afford the desired compound **5a** with 69% of yield. Same procedure repeated for remaining all the compounds.

4.2 | Typical procedure for synthesis of 2-(4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy) phenyl)isoindoline-1,3-dione derivatives (9a-f)

Synthesis of compounds (**9a-f**) (Scheme 2) was also involved in three steps. In the first step, dissolved the equimolar mixture of pthalic anhydride (**1**, 2 g, 0.013 mol) and 4-amino phenol (**6**, 1.47 g, 0.013 mol) in 20 ml of acetic acid, stirred at 100°C for 3 hours and poured the reaction mixture in crushed ice and filtered the solid compound (**7**) with 85% of yield. In step 2, to a stirred solution of compound **7** (2 g, 0.008 mol) in 15 ml of DMF was added potassium carbonate (3.46 g, 0.025 mol). Then, added propargyl bromide (1.18 g, 0.01 mol) and stirred at RT for 2 hours to afforded the desired compound 2-(4-(prop-2-yn-1-yloxy) phenyl)isoindoline-1,3-dione (**8**) with 90% of yield. Finally,



SCHEME 1 Conditions: (a) acetic acid, 100°C, 3 hours; (b) sodium borohydride, methanol, 0°C- RT, 2 hours; (c) sodium hydride, 0°C- RT, 2 hours, 1,3-di bromo propane/1,4-dibromo butane/1,5-dibromo pentane.



SCHEME 2 Conditions: (a) Acetic acid, 100°C, 3 hours; (b) K_2CO_3, Propagyl bromide, DMF, RT, 3 hours; (c) Azides, 10 mol% of sodium ascorbate, 10 mol% of $CuSO_4.H_2O$, DMF: Water (1:1), RT, 10 to 12 hours.

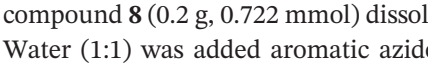
compound **8** (0.2 g, 0.722 mmol) dissolved in 5 ml of DMF: Water (1:1) was added aromatic azide (0.1 g, 0.8 mmol), sodium ascorbate (10 mol%), copper sulphate (10 mol%) and stirred it at room temperature for 10 hours gave compound **9a** with yield (79%). Same procedure repeated for remaining all compounds.

4.3 | Typical procedure for synthesis of (1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl) benzoate (13a-e)

Synthesis of compounds (**13a-e**) (Scheme 3) was also involved in three steps. First step, dissolved the equimolar mixture of pthalic anhydride (**1**, 2 g, 0.013 mol) and 4-amino benzoic acid (**10**, 1.85 g, 0.013 mol) in 20 mL of acetic acid, stirred at 100°C for 3 hours and poured into crushed ice and filtered the solid compound (**11**) with 83% of yield. Then, to a stirred solution of 4-(1, 3-dioxoisoindolin-2-yl) benzoic acid (**11**, 2 g, 0.0074 mol) in 15 mL of DMF was added K_2CO_3 (3.1 g, 0.0224 mol), propargyl bromide (1.06 g, 0.0089 mol), and stirred at RT for 3 hours gave prop-2-yn-1-yl 4-(1,3-dioxoisoindolin-2-yl) benzoate (**12**) with 87% of yield. Finally, compound **12** (200 mg, 0.655 mmol) was treated with 1-azido 4-methyl benzene (95 mg, 0.721 mmol) in the presence of 10 mol% of sodium ascorbate and 10 mol% copper sulphate in 5 mL of DMF:Water (1:1) mixture was stirred at RT for 10 hours afforded the desired product (1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl) benzoate (**13**) in 78% of yield. Same procedure repeated for remaining all the compounds.

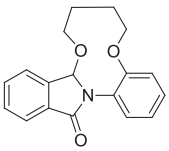
5 | SPECTRAL DATA

5.1 | 7,8-Dihydro-6*H*-benzo[4,5][1,6,3] dioxazonino[2,3-a]isoindol-14(9a*H*)-one (5a)

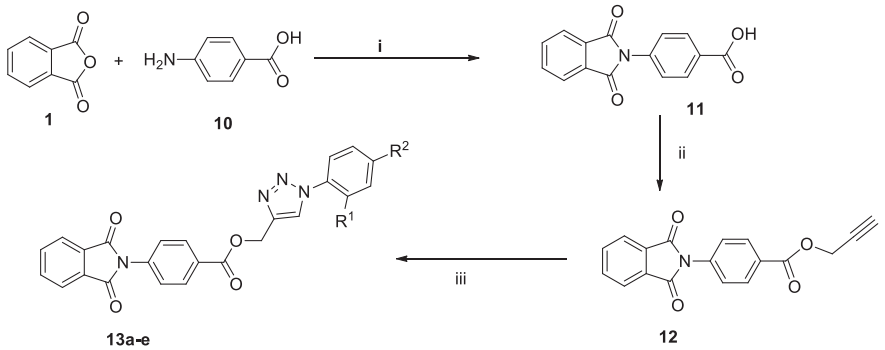


Yield 69%, mp 68°C-70°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 3.61-3.65 (m, 1H), 3.85-3.90 (m, 1H), 4.55-4.59 (m, 2H), 5.67-5.77 (m, 1H), 5.89-5.99 (m, 1H), 6.51 (s, 1H), 6.99-7.02 (d, 2H, J = 8.28 Hz), 7.30-7.39 (m, 2H), 7.54-7.66 (m, 3H), 7.92 (d, 1H, J = 7.52 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz), δ ppm: 20.5, 64.9, 69.2, 87.6, 113.3, 117.1, 117.2, 123.6, 123.9, 124.6, 129.8, 130.5, 130.6, 132.3, 132.5, 133.9, 141.5, 152.0, 167.2. ESI Mass m/z at 282 $[M + H]^+$. Elemental analysis calculated for $C_{17}H_{15}NO_3$; C, 72.58; H, 5.37; N, 4.98. Found %: C, 72.67; H, 5.44; N, 5.03.

5.2 | 6,7,8,9-Tetrahydrobenzo[4,5][1,6,3] dioxazecino[2,3-a]isoindol-15(10a*H*)-one (5b)

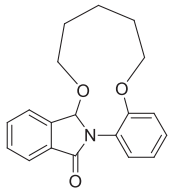


Yield 67%, mp 206°C-208°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 1.24-1.29 (m, 1H), 1.37-1.66 (m, 1H), 1.74-1.91 (m, 1H), 3.14-3.18 (m, 1H), 3.67-3.73 (m, 1H), 4.11-4.20 (m, 1H), 4.47-4.51 (m, 1H), 5.04-5.13 (m, 1H), 6.05 (s, 1H), 7.06-7.10 (m, 1H), 7.17-7.25 (m, 2H), 7.37-7.42 (m, 1H), 7.54-7.64 (m, 3H), 7.91-7.94 (m, 1H). ESI Mass m/z at 296 $[M + H]^+$. Elemental analysis calculated for $C_{18}H_{17}NO_3$; C, 73.20; H, 5.80; N, 4.74. Found %: C, 73.27; H, 5.84; N, 4.79.



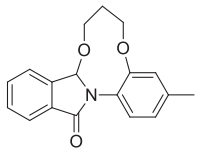
SCHEME 3 Conditions: (a) acetic acid, 100°C, 3 hours; (b) K_2CO_3, Propagyl bromide, DMF, RT, 3 h; (c) Azides, 10 mol % of sodium ascorbate, 10 mol% of $CuSO_4$. H_2O, DMF:Water (1:1), RT, 10 to 12 hours.

5.3 | 7,8,9,10-Tetrahydro-6*H*-benzo[4,5][1,6,3]dioxaazacycloundecino[2,3-a]isoindol-16(11a*H*)-one (5c)



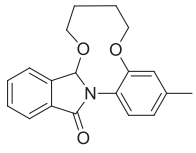
Yield 61%, mp 188°C-190°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 1.35-1.46 (m, 2H), 1.61-1.68 (m, 3H), 1.82-1.89 (m, 1H), 2.93-2.97 (m, 1H), 3.77-3.88 (m, 2H), 4.24-4.27 (m, 1H), 6.14 (s, 1H), 6.95-7.03 (m, 2H), 7.15-7.17 (d, 1H, J = 7.52 Hz), 7.33-7.37 (m, 1H), 7.55-7.66 (m, 3H), 7.92 (d, 1H, J = 7.52 Hz). ESI Mass m/z at 310 $[M + H]^+$. Elemental analysis calculated for $C_{19}H_{19}NO_3$; C, 73.77; H, 6.19; N, 4.53. Found %: C, 73.84; H, 6.24; N, 4.59.

5.4 | 3-Methyl-7,8-dihydro-6*H*-benzo[4,5][1,6,3]dioxazonino[2,3-a]isoindol-14(9a*H*)-one (5d)



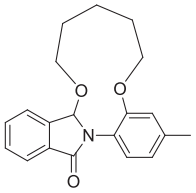
Yield 79%, mp 70°C-72°C. ^{13}C NMR ($CDCl_3$, 100 MHz), δ ppm: 20.5, 64.9, 69.2, 87.6, 113.3, 117.1, 117.2, 123.6, 123.9, 124.6, 129.5, 129.8, 130.5, 130.6, 132.3, 132.5, 133.9, 141.5, 152.0, 167.2. ESI Mass m/z at 296 $[M + H]^+$. Elemental analysis calculated for $C_{18}H_{17}NO_3$; C, 73.20; H, 5.80; N, 4.74. Found %: C, 73.27; H, 5.84; N, 4.79.

5.5 | 3-Methyl-6,7,8,9-tetrahydrobenzo[4,5][1,6,3]dioxazecino[2,3-a]isoindol-15(10a*H*)-one (5e)



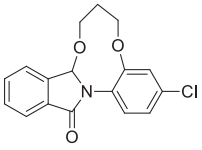
Yield 76%, mp 152°C-154°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 1.33-1.42 (m, 1H), 1.45-1.53 (m, 1H), 1.74-1.91 (m, 2H), 2.31 (s, 3H), 3.12-3.16 (m, 1H), 3.67-3.73 (m, 1H), 4.14 (t, 1H, J = 11.54 Hz), 4.43-4.47 (m, 1H), 6.05 (s, 1H), 7.04 (d, 1H, J = 1.75 Hz), 7.06-7.09 (d, 1H, J = 8.53 Hz), 7.18 (m, 1H), 7.53-7.63 (m, 3H), 7.92 (d, 1H, J = 7.20 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz), δ ppm: 20.5, 23.1, 28.6, 60.8, 71.7, 89.2, 117.0, 123.7, 124.0, 127.7, 129.8, 130.5, 130.6, 131.9, 132.1, 133.1, 140.6, 153.7, 167.4. ESI Mass m/z at 310 $[M + H]^+$. Elemental analysis calculated for $C_{19}H_{19}NO_3$; C, 73.77; H, 6.19; N, 4.53. Found %: C, 73.86; H, 6.24; N, 4.59.

5.6 | 3-Methyl-7,8,9,10-tetrahydro-6*H*-benzo[4,5][1,6,3]dioxaazacycloundecino[2,3-a] isoindol-16 (11a*H*)-one (5f)



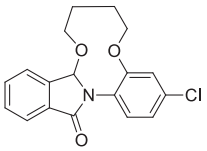
Yield 72%, mp 128°C-130°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 1.25-147 (m, 2H), 1.52-1.68 (m, 4H), 1.79-1.86 (m, 1H), 2.28 (s, 3H), 2.93-2.97 (m, 1H), 3.76-3.84 (m, 2H), 4.22-4.26 (m, 1H), 6.14 (s, 1H), 6.85 (d, 1H, J = 8.28 Hz), 6.97 (d, 1H, J = 1.75 Hz), 7.13-7.15 (d, 1H, J = 8.28 Hz), 7.54-7.62 (m, 2H), 7.92 (d, 1H, J = 7.27 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz), δ ppm: 20.3, 21.5, 26.8, 29.3, 58.6, 69.8, 90.0, 112.8, 123.6, 123.9, 125.5, 129.8, 130.1, 130.3, 132.1, 132.7, 141.5, 155.3, 168.0. ESI Mass m/z at 324 $[M + H]^+$. Elemental analysis calculated for $C_{20}H_{21}NO_3$; C, 74.28; H, 6.55; N, 4.33. Found %: C, 74.37; H, 6.59; N, 4.39.

5.7 | 3-Chloro-7,8-dihydro-6*H*-benzo[4,5][1,6,3]dioxazonino[2,3-a]isoindol-14(9a*H*)-one (5g)



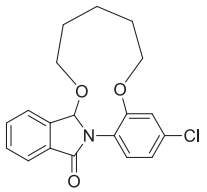
Yield 62%, mp 96°C-98°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 0.81-0.86 (m, 1H), 3.57-3.71 (m, 1H), 5.08 (m, 2H), 5.62-5.72 (m, 2H), 6.57 (s, 1H), 7.08 (d, 1H, J = 8.78 Hz), 7.23 (d, 1H, J = 8.78 Hz), 7.31 (d, 1H, J = 2.25 Hz), 7.62-7.74 (m, 3H), 7.93 (d, 1H, J = 7.52 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz), δ ppm: 29.7, 64.6, 87.9, 117.9, 121.7, 123.7, 124.2, 125.8, 128.4, 130.7, 131.2, 132.9, 133.4, 141.4, 150.0, 168.0. ESI Mass m/z at 316 $[M + H]^+$. Elemental analysis calculated for $C_{17}H_{14}NClO_3$; C, 64.67; H, 4.47; N, 4.44. Found %: C, 64.74; H, 4.52; N, 4.49.

5.8 | 3-Chloro-6,7,8,9-tetrahydrobenzo[4,5][1,6,3]dioxazecino[2,3-a]isoindol-15(10a*H*)-one (5h)



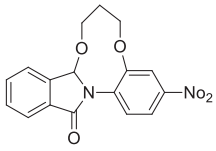
Yield 63%, mp 174°C-176°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 1.39-1.51 (m, 2H), 1.75-1.84 (m, 2H), 3.14-3.18 (m, 1H), 3.62-3.68 (m, 1H), 4.15-4.21 (m, 1H), 4.41-4.45 (m, 1H), 6.05 (m, 1H), 7.11 (d, 1H, J = 8.78 Hz), 7.25 (m, 1H), 7.35-7.38 (d, 1H, J = 8.78 Hz), 7.55-7.66 (m, 3H), 7.82 (d, 1H, J = 8.53 Hz). ESI Mass m/z at 330 $[M + H]^+$. Elemental analysis calculated for $C_{18}H_{16}ClNO_3$; C, 65.56; H, 4.89; N, 4.25. Found %: C, 65.64; H, 4.93; N, 4.29.

5.9 | 3-Chloro-7,8,9,10-tetrahydro-6*H*-benzo[4,5][1,6,3]dioxaazacycloundecino[2,3-a]isoindol-16(11a*H*)-one (5i)



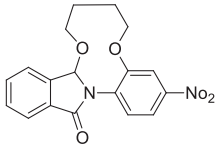
Yield 59%, mp 170°C-172°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 0.79-0.88 (m, 1H), 1.28-1.42 (m, 3H), 1.62 (m, 1H), 1.82-1.88 (m, 1H), 2.94–2.98 (m, 1H), 3.72-3.84 (m, 2H), 4.23-4.27 (m, 1H), 6.14 (s, 1H), 6.88 (d, 1H, J = 8.78 Hz), 7.17 (d, 1H, J = 2.76 Hz), 7.30-7.33 (d, 1H, J = 8.78 Hz), 7.55-7.73 (m, 3H), 7.92 (d, 1H, J = 8.53 Hz). ESI Mass m/z at 344 $[M + H]^+$. Elemental analysis calculated for $C_{19}H_{18}ClNO_3$; C, 66.38; H, 5.28; N, 4.07. Found %: C, 66.75; H, 5.32; N, 4.12.

5.10 | 3-Nitro-7,8-dihydro-6*H*-benzo[4,5][1,6,3]dioxazonino[2,3-a]isoindol-14(9a*H*)-one (5j)



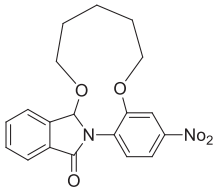
Yield 49%, mp 128°C-130°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 3.63-3.72 (m, 2H), 5.07-5.10 (m, 2H), 5.12-5.14 (m, 1H), 5.61-5.71 (m, 1H), 6.70 (s, 1H), 7.21 (d, 1H, J = 9.03 Hz), 7.65-7.78 (m, 3H), 7.96 (d, 1H, J = 7.27 Hz), 8.16-8.18 (d, 1H, J = 9.03 Hz), 8.31 (d, 1H, J = 2.51 Hz). ESI Mass m/z at 328 $[M + H]^+$. Elemental analysis calculated for $C_{17}H_{14}N_2O_5$; C, 62.57; H, 4.32; N, 8.59. Found %: C, 62.66; H, 4.37; N, 8.67.

5.11 | 3-Nitro-6,7,8,9-tetrahydrobenzo[4,5][1,6,3]dioxazecino[2,3-a]isoindol-15(10a*H*)-one (5k)



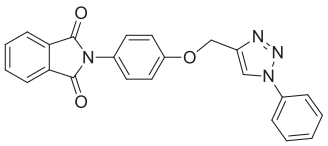
Yield 45%, mp 150°C-152°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 1.77-1.86 (m, 1H), 2.11-2.16 (m, 1H), 3.07-3.25 (m, 1H), 3.59-3.64 (m, 1H), 4.30-4.38 (m, 1H), 4.51-4.55 (m, 1H), 4.87-4.94 (m, 1H), 5.45-5.52 (m,1H), 6.07 (s, 1H), 6.68 (d, 1H, J = 9.53 Hz), 7.20-7.24 (m, 1H), 7.58-7.69 (m, 3H), 7.93 (m, 1H), 8.22 (d, 1H, J = 2.76 Hz). ESI Mass m/z at 342 $[M + H]^+$. Elemental analysis calculated for $C_{18}H_{16}N_2O_5$; C, 63.52; H, 4.74; N, 8.23. Found %: C, 63.59; H, 4.78; N, 8.28.

5.12 | 3-Nitro-7,8,9,10-tetrahydro-6*H*-benzo[4,5][1,6,3]dioxaazacycloundecino[2,3-a]isoindol-16(11a*H*)-one (5l)



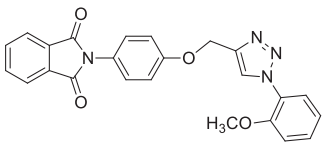
Yield 46%, mp 160°C-162°C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm: 1.37-1.58 (m, 2H), 1.62-1.70 (m, 2H), 1.84-1.90 (m, 1H), 3.05-3.15 (m, 2H), 3.23-3.27 (m, 1H), 4.80-4.86 (m, 1H), 5.54-5.64 (m, 1H), 6.18 (s, 1H), 6.68 (d, 1H, J = 7.78 Hz), 7.19-7.23 (m, 1H), 7.66-7.77 (m, 2H), 7.95-7.97 (m, 1H), 8.15-8.18 (m, 1H), 8.30 (d, 1H, J = 2.76 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz), δ ppm: 24.5, 28.3, 29.6, 32.1, 33.3, 62.7, 62.8, 88.1, 88.2, 115.0, 120.4, 120.5, 120.7, 120.8, 123.7, 123.9, 124.4, 124.5, 125.0, 130.7, 130.8, 130.9, 133.9, 137.3, 141.4, 157.1, 16.7. ESI Mass m/z at 356 $[M + H]^+$. Elemental analysis calculated for $C_{19}H_{18}N_2O_5$; C, 64.40; H, 5.12; N, 7.91. Found %: C, 64.51; H, 5.17; N, 7.98.

5.13 | 2-(4-((1-Phenyl-1*H*-1,2,3-triazol-4-yl) methoxy)phenyl)isoindoline-1,3-dione (9b)



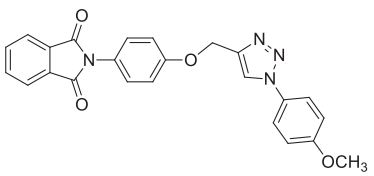
Yield 81%, mp 183°C-185°C. IR (cm^{-1}) 1694, 3158. ^1H NMR (400 MHz, $CDCl_3$), δ ppm: 5.36 (s, 2H), 7.15 (d, 2H, J = 9.03 Hz), 7.36 (d, 2H, J = 9.03 Hz), 7.46 (m, 1H), 7.54 (m, 2H), 7.49-7.81 (m, 4H), 7.95 (m, 2H), 8.08 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ ppm: 62.3, 115.3, 120.7, 121.0, 123.7, 124.9, 128.9, 129.8, 131.7, 134.3, 136.9, 144.7, 157.7, 167.5. ESI Mass m/z at 397 $[M + H]^+$. Elemental analysis calculated for $C_{23}H_{16}N_4O_3$; C, 69.69; H, 4.07; N, 14.13. Found %: C, 69.76; H, 4.14; N, 14.19.

5.14 | 2-(4-((1-(2-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)isoindoline-1,3-dione (9b)



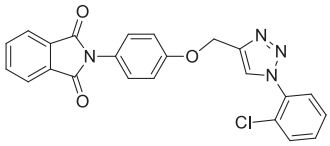
Yield 79%, mp 170°C-172°C. IR (cm^{-1}): 1678, 3000. ^1H NMR (400 MHz, $CDCl_3$), δ ppm: 3.91 (s, 3H), 5.59 (s, 2H), 7.10 (m, 2H), 7.43 (m, 1H), 7.58 (d, 2H, J = 8.78 Hz), 7.78-7.82 (m, 3H), 7.96-8.01 (m, 2H) 8.21 (d, 2H, J = 8.78 Hz), 8.26 (s, 1H). ^{13} C NMR (100 MHz, $CDCl_3$), δ ppm: 56.0, 62.3, 112.2, 115.4, 121.2, 123.7, 124.8, 125.1, 125.5, 126.2, 128.0, 130.2, 131.8, 134.3, 143.2, 151.1, 157.9, 167.9. ESI Mass m/z at 427 $[M + H]^+$. Elemental analysis calculated for $C_{24}H_{18}N_4O_4$; C, 67.60; H, 4.25; N, 13.14. Found %: C, 67.69; H, 4.31; N, 13.19.

5.15 | 2-(4-((1-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)isoindoline-1,3-dione (9c)



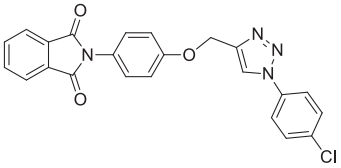
Yield 80% mp 225°C-227°C. IR (cm^{-1}) 1678, 3064. ^1H NMR (400 MHz, $CDCl_3$), δ ppm: 3.87 (s, 3H), 5.35 (s, 2H), 7.03 (d, 2H, J = 9.03 Hz), 7.15 (d, 2H, J = 9.03 Hz), 7.36 (d, 2H, J = 9.03 Hz), 7.65 (d, 2H, J = 9.03 Hz), 7.79 (q, 2H, J = 3.01 Hz), 7.95 (q, 2H, J = 3.01 Hz), 7.99 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ ppm: 55.6, 62.3, 114.8, 115.3, 121.1, 1222.3, 123.7, 124.9, 128.0, 130.4, 131.8, 134.3, 144.4, 157.8, 159.9, 167.5. ESI Mass m/z at 427 $[M + H]^+$. Elemental analysis calculated for $C_{24}H_{18}N_4O_4$; C, 67.60; H, 4.25; N, 13.14. Found %: C, 67.71; H, 4.29; N, 13.21.

5.16 | 2-(4-((1-(2-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)isoindoline-1,3-dione (9d)



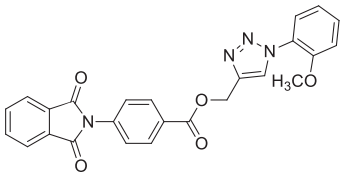
Yield 73%, mp 260°C-262°C. IR (cm^{-1}) 1701, 2933. ^1H NMR (400 MHz, $CDCl_3$), δ ppm: 5.35 (s, 2H), 7.14 (d, 2H, J = 9.03 Hz), 7.36 (d, 2H, J = 9.03 Hz), 7.42-7.50 (m, 2H), 7.65-7.67 (m, 1H), 7.78-7.80 (q, 2H, J = 3.01 Hz), 7.82 (m, 1H), 7.95 (q, 2H, J = 3.01 Hz), 8.07 (s, 1H). ESI Mass m/z at 431 $[M + H]^+$. Elemental analysis calculated for $C_{23}H_{15}ClN_4O_3$; C, 64.12; H, 3.51; N, 13.00. Found %: C, 64.18; H, 3.58; N, 13.06.

5.17 | 2-(4-((1-(4-Chlorophenyl)-1*H*-1,2,3-triazole-1-yl)methoxy)phenyl)isoindoline-1,3-dione (9e)



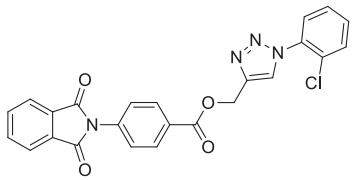
Yield 70%, mp 260°C-262°C. IR (cm^{-1}) 1693, 2956. ^1H NMR (400 MHz, $CDCl_3$), δ ppm: 5.35 (s, 2H), 7.14 (d, 2H, J = 9.03 Hz), 7.36 (d, 2H, J = 9.03 Hz), 7.52 (d, 2H, J = 8.78 Hz), 7.71(d, 2H, J = 9.03 Hz), 7.79 (q, 2H, J = 3.01 Hz), 7.93 (q, 2H, J = 3.01 Hz), 8.05 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ ppm: 62.2, 115.3, 120.9, 121.8, 123.7, 124.9, 128.1, 130.0, 131.7, 134.4, 134.7, 135.4, 144.9, 157.7, 167.5. ESI Mass m/z at 431 $[M + H]^+$. Elemental analysis calculated for $C_{23}H_{15}ClN_4O_3$; C, 64.12; H, 3.51; N, 13.00. Found %: C, 64.21; H, 3.56; N, 13.12.

5.18 | (1-(2-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl)benzoate (13a)



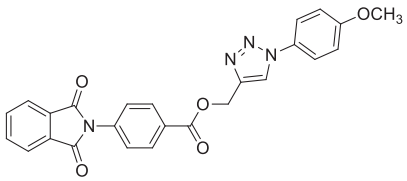
Yield 78%, mp. 174°C-176°C. ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 3.90 (s, 3H), 5.59 (s, 2H), 7.08-7.13 (m, 2H), 7.41-7.45 (m, 1H), 7.59 (d, 2H, J = 8.78 Hz), 7.78-7.82 (m, 3H), 7.96-7.98 (m, 2H), 8.21 (d, 2H, J = 8.78 Hz), 8.26 (s, 1H). ESI Mass m/z at 455 $[M + H]^+$. Elemental analysis calculated for $C_{25}H_{18}N_4O_5$; C, 66.08; H, 3.99; N, 12.33. Found %: C, 66.12; H, 4.08; N, 12.42.

5.19 | (1-(2-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl) benzoate (13b)



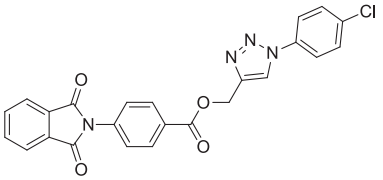
Yield 62%, mp 162°C-164°C. ^{1}H NMR (400 MHz, $CDCl_3$), δ ppm: 5.61 (s, 2H), 7.33-7.50 (m, 2H), 7.58-7.65 (m, 4H), 7.80-7.84 (m, 2H), 7.96-7.98 (m, 2H), 8.15 (s, 1H), 8.21 (d, 2H, J = 8.78 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ ppm: ESI Mass m/z at 459 $[M + H]^+$. Elemental analysis calculated for $C_{24}H_{15}ClN_4O_4$; C, 62.82; H, 3.29; N, 12.29.

5.20 | (1-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl)benzoate (13c)



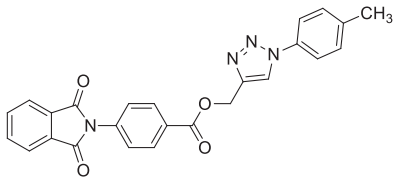
Yield 73%, mp 170°C-172°C. ^{1}H NMR (400 MHz, $CDCl_3$), δ ppm: 3.87 (s, 3H), 5.58 (s, 2H), 7.02 (d, 2H, J = 8.03 Hz), 7.59-7.69 (m, 4H), 7.82 (m, 2H), 7.86 (m, 2H), 8.06 (s, 2H), 8.20 (d, 2H, J = 8.28 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ ppm: 55.6, 58.3, 114.8, 122.3, 123.9, 125.9, 128.8, 130.6, 131.5, 134.7, 136.1, 159.9, 165.7, 166.7. ESI Mass m/z at 455 $[M + H]^+$. Elemental analysis calculated for $C_{25}H_{18}N_4O_5$; C, 66.08; H, 3.99; N, 12.33. Found %: C, 66.19; H, 4.04; N, 12.37.

5.21 | (1-(4-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methyl 4-(1,3-dioxoisoindolin-2-yl) benzoate (13d)



Yield 61%, mp 164°C-166°C. ^{1}H NMR (400 MHz, $CDCl_3$), δ ppm: 5.58 (s, 3H), 7.50-7.52 (d, 2H, J = 9.03 Hz), 7.59-7.61 (d, 2H, J = 8.28 Hz), 7.70-7.72 (d, 2H, J = 8.28 Hz), 7.81-7.83 (m, 2H), 7.96-7.98 (m, 2H), 8.12 (s, 1H), 8.19-8.21 (d, 2H, J = 8.78 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ ppm: 56.3, 58.2, 123.9, 125.9, 126.1, 127.8, 127.9, 128.6, 128.8, 130.6, 130.8, 130.9, 131.5, 134.7, 136.1, 142.6, 165.6, 166.7. ESI Mass m/z at 459 $[M + H]^+$. Elemental analysis calculated for $C_{24}H_{15}ClN_4O_4$; C, 62.82; H, 3.29; N, 12.21. Found %: C, 62.89; H, 3.35; N, 12.29.

5.22 | (1-(*p*-Tolyl)-1*H*-1,2,3-triazol-4-yl) methyl 4-(1,3-dioxoisoindolin-2-yl)benzoate (13e)



Yield 76%, mp 142°C-144°C. ^{1}H NMR (400 MHz, $CDCl_3$), δ ppm: 2.68 (s, 3H), 5.60 (s, 2H), 7.60-7.68 (m, 3H), 7.81-7.83 (m, 2H), 7.96-8.06 (m, 4H), 8.20-8.23 (m, 3H), 8.31 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ ppm: 56.0, 58.3, 112.2, 121.2, 123.9, 125.5, 125.9, 126.1, 128.9, 130.2, 131.5, 134.7, 136.0, 142.1, 151.1, 165.7, 166.7. ESI Mass m/z at 439 $[M + H]^+$. Elemental analysis calculated for $C_{25}H_{18}N_4O_4$; C, 68.49; H, 4.14; N, 12.78. Found %: C, 68.53; H, 4.16; N, 12.83.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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