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Microwave-assisted multicomponent reaction in water leading to highly regioselective formation of benzo[f]azulen-1-ones

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Abstract

Microwave-assisted three-component reaction has been established for the regioselective synthesis of benzo[f]azulen-1-ones. The reaction was performed in aqueous media under microwave irradiation by using readily available and inexpensive starting materials. A total of 38 examples were examined to show a broad substrate scope and good overall yields (70–89%). The present new synthesis shows attractive green chemistry characteristics, such as the use of water as reaction media, concise one-pot conditions, short reaction periods (7–24 min), easy work-up/purification and reduced waste production without the use of any strong acids or metal promoters.

Keywords

Tetronic acid; Benzo[f]azulen-1-ones; Microwave-assisted multicomponent reaction; Aqueous media; Green synthesis

1. Introduction

Heterocycles containing benzodiazepine rings belong to important building blocks because of their remarkable depressant activity in central nervous system¹ and their being one of the most widely prescribed class of psychotropics.^{1h-i} In addition, some of these compounds also possess bioactivities on analgesic, sedative and antidepressive as well as hypnotic activities.² On the other hand, the derivatives of tetronic acid (tetrahydrofuran-2,4-dione) play an essential role in medicinal chemistry³ by serving as HIV-1 protease inhibiting⁴, anti-inflammatory,⁵ antifungal,⁶ antibiotic,⁷ insecticidal,⁸ analgesic,⁹ anticoagulant¹⁰ and antiepileptic¹¹ agents. Consequently, benzoazulen-1-one derivatives containing both

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Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.

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benzodiazepine and tetronic acid motifs would provide novel leading structures for combinatorial drug-discovery research.

A careful literature survey revealed that benzo[f]azulen-1-one derivatives have been synthesized by the condensation reaction of 4-(2-aminophenylamino)furan-2(5*H*)-one with aldehyde in normal organic solvents.¹² However, the substrate scope of this reaction is limited. It also suffered by other shortcomings, such as multiple steps, long reaction times, low overall yields and environmental unfriendly and uneconomical. So far, there have been a few benzo[f]azulen-1-one compounds produced via this method. The continuing search for new efficient approaches to benzo[f]azulen-1-ones in terms of mild reaction conditions, operational simplicity, economic viability, eco-friendliness and selectivity remains challenging.

In the past several years, our groups and several others have developed a series of multicomponent domino reactions (MDRs) that can provide easy accesses to multifunctionalized heterocyclic structures of chemical and pharmaceutical interest.^{13–16} Especially, we established a new four-component domino reaction for an efficient synthesis of multifunctionalized quinazoline derivatives.^{13a} The reaction is easily performed by simply mixing readily available starting materials, aromatic aldehydes, cyclopentanone and cyanoacetamide with K₂CO₃ in ethylene glycol under microwave (MW) irradiation. Interestingly, when aliphatic aldehydes were employed to replace their aromatic counterparts for the above MDR reaction, the reaction was found to undergo along another pathway leading to the formation of multi-functionalized tricyclo[6.2.2.0^{1,6}]dodecanes.^{13b} Recently, we have also found that the MDR of Meldrum's acid, aromatic aldehydes and electron-rich heteroaryl-amines in aqueous phase under microwave irradiation (MW) led to the multifunctionalized spiro{[1,3]dioxanes-pyridine}-4,6-dione with high chemo- regio- and stereoselectivity and good yields.^{13d}

As a continuation of our research devoted to the development of multicomponent domino reactions,^{13–15} in this communication we would like to report a new green chemistry approach to benzo[f]azulen-1-one derivatives that are of chemical and biomedical importance (Scheme 1). This reaction was achieved by reacting benzene-1,2-diamines, tetronic acid and aldehydes in aqueous phase under microwave irradiation without use of any metal catalyst as represented in Scheme 1.

Results and discussion

We started this methodology by subjecting 3,4-diaminobenzoic acid **1a** to the reaction with 4-chlorobenzaldehyde **2a** and tetronic acid **3** as the model case for condition optimization. As shown in Table 1, the use of glacial acetic acid (HOAc) as reaction media at 90 °C allowed the direct conversion of 3,4-diaminobenzoic acid **1a** into the corresponding benzo[f]azulen-1-ones **4a** in a chemical yield of 55% under microwave irradiation (Table 1, entry 4). Other organic solvents, such as benzene, DCE, DMF, THF, ethanol and glycol gave much lower yields of 10% - 45% at the same temperature (Table 1, entries 1–3); this is due to the fact that the benzo[d]imidazoles **5** were generated as by-products. Since water is an efficient absorber for microwave irradiation, it often leads to many successful reactions under environmentally friendly conditions.^{17–18} Under this aqueous system, the three-component reaction of **1a** with **2a** and **3** resulted in benzo[f]azulen-1-ones **4a** with a chemical yield of 51%. The reaction proceeded rapidly to completion at 110 °C within a few minutes. Increasing reaction temperature did not improve chemical yields. Pleasantly, we found that a higher yield of **4a** (86%) was obtained when the reaction was conducted in presence of 0.1 equivalent of HOAc at 110 °C.

We then investigated the substrate scope of this reaction by subjecting a series of aromatic aldehyde **2b–i** to the reaction with 3,4-diaminobenzoic acid **1a** under the optimal condition. As shown in Table 2, the reaction of thiophene-2-carbaldehyde with 3,4-diaminobenzoic acid **1a** was finished within 12 min to give thienyl-substituted benzo[f]azulen-1-ones **4h** in 85% yield. Similarly, benzo[f]azulen-1-ones **4b–g** were formed within 12–15 min in good to excellent yields of 74–89% (Table 2, entries 2–7). Moreover, aliphatic aldehydes, such as 2-phenylacetaldehyde (Table 2, entry 9) still displayed high reactivity and clean conversion under this condition. The similar situation exists for the use of 4-chlorobenzene-1,2-diamine **1b** for reactions that occurred rapidly to give the desired products **4j–4n** in 76–84% yields (Table 2, entries 10–14). It is worth noting that these reactions showed high regioselectivity; only one single regioisomer was generated when 3,4-diaminobenzoic acid and 4-chlorobenzene-1,2-diamine were employed as substrates. The reason for this excellent selectivity is that the amino group attached on *meta* position of carboxyl group on the phenyl ring shows higher nucleophilic than that on *para* position, favoring to condense with tetronic acid. While the halogen substitution has an ortho-para directing effect, the amino group on the para position of chloro group shows higher reactivity than that on meta-position, preferring to form enaminones from the reaction with tetronic acid.

After we achieved the above mono-substituted benzene-1,2-diamine-based multicomponent reaction, we then subjected symmetric benzene-1,2-diamine (including **1c** and **1d**) to the reaction with aromatic aldehydes **2** and tetronic acid under the similar conditions. As shown in Table 3, the corresponding products **4** were generated in good to excellent yields of 81–92% (Scheme 2). The reaction is compatible with various substrates including aldehydes with aromatic, heteroaromatic and aliphatic ones and aromatic diamine component with both Cl and COOH substituents. The products has been unambiguously determined by X-ray structural analysis of single crystals of **4g** and **4u**, which were obtained by carefully evaporating solvents (Fig. 1 and 2).

To expand the substrate scope of this reaction, the 2-formylbenzoic acid **2v** and 2-formyl-4,5-dimethoxybenzoic acid **2w** were employed to react with benzene-1,2-diamine (**1c**, **1d**, or 4,5-dimethylbenzene-1,2-diamine **1e**) and tetronic acid **3** (Scheme 3). To our delight, under the above optimized conditions, these reactions proceeded smoothly to give pentacyclic isoindole-fused furo[1,4]diazepines **5a–5f** in good to excellent yields (Table 4, entries 1–6). Excellent regioselectivity was observed in this three-component reaction involving 3,4-diaminobenzoic acid and 2-formylbenzoic acid (Table 4, entries 7–8). It is worth noting that this result is significant with no literature precedent regarding the synthesis of highly functionalized isoindole-fused furo[1,4]diazepines.

Similar to our previous multicomponent domino processes,¹³ the present reaction also showed *the following attractive characteristics*: (1) fast reaction rates which enable the reaction to be completed within 7–17 min, which can save energy and manpower for future industrial production; (2) the environmentally friendly process in which water is used as a solvent; (3) the convenient work-up which only needs simple filtration since the products directly precipitate out after the reaction is finished, which belongs to GAP chemistry;^{19–20} (4) readily available starting materials of aldehydes, substituted benzene-1,2-diamine and tetronic acid.

In according to a similar mechanism,¹² the formation of **4** is likely to proceed *via* initial condensation of benzene-1,2-diamine **1** and tetronic acid **3** to give enaminone **6**. The following addition of aldehydes **2** to enaminone **6** furnishes the formation of intermediate **7** which is then converted into the final product **4** through intramolecular cyclization (Scheme 4). The carbonyl substituent on the aromatic ring **2** was dehydrated upon the treatment with amino group, leading to the formation of pentacyclic isoindole-fused furo[1,4]diazepines.

Based on this mechanism, the regioselectivity is controlled by the strong nucleophilicity of amino group on starting material **1**, *i.e.*, the formation of **4a-4n** depends on the higher nucleophilicity of the amino group in the meta position of carboxyl group than in that on para position.

Conclusion

In conclusion, a new microwave-assisted multi-component reaction have been established to afford benzo[f]azulen-1-one and isoindole-fused furo[1,4]diazepine derivatives that can serve as versatile building blocks for both organic and medicinal research. The reactions were conducted in aqueous solution under microwave irradiation using readily available and inexpensive starting materials. The directing effects of substituents on benzene-1,2-diamine ring have been proven to control regioselectivity efficiently. This green synthesis shows several attractive characteristics such as the use of water as reaction media, concise conditions, short reaction periods, easy work-up, and reduced waste production without the use of any strong acids or metal promoters.

Experimental section

Microwave irradiation was carried out with microwave oven Emrys™ Creator from Personal Chemistry, Uppsala, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in cm^{-1} . ^1H NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in $\text{DMSO}-d_6$ with chemical shift (δ) given in ppm relative to TMS as internal standard. HRMS (ESI) was determined by using microTOF-Q II HRMS/MS instrument (Bruker). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

General procedure for the synthesis of benzo[f]azulen-1-ones **4a**

In a 10-mL reaction vial, the benzene-1,2-diamine **1a** (1 mmol), tetronic acid **3** (1 mmol), acetic acid (0.1 mmol) and water (2 mL) were mixed and then stirring for 30 min. Subsequently, the aldehydes **2a** (1 mmol) was added to the reaction mixture, and the reaction vial was capped and pre-stirring for 20 second. The mixture was subjected to microwave irradiation at 200W (initial power 100W, maximum power 200W) at 110 °C, for a given time. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature, filtered to give the crude product, which was further washed by 50% EtOH to give pure product **4a**.

10-(4-Chlorophenyl)-1-oxo-3,4,9,10-tetrahydro-1H-2-oxa-4,9-diaza-benzo[f]azulene-6-carboxylic acid **4a**

Pale white solid, Mp: 281–282 °C

IR(KBr): 3373, 3323, 3134, 1725, 1691, 1672, 1601, 1571, 1390, 1197, 1164, 1133, 1051, 1012, 832, 820, cm^{-1}

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 12.53 (s, 1H, COOH), 10.10 (s, 1H, NH), 7.57 (d, $J = 1.6$ Hz, 1H, ArH), 7.31–7.27 (m, 3H, ArH), 7.16 (d, $J = 8.8$ Hz, 2H, ArH), 6.71–6.68 (m, 2H, ArH and NH), 5.08 (d, $J = 4.4$ Hz, 1H, CH), 4.91 (s, 2H, CH_2)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{18}\text{H}_{14}\text{ClN}_2\text{O}_4$: 357.0637; found: 357.0649.

10-(4-Bromophenyl)-1-oxo-3,4,9,10-tetrahydro-1H-benzo[b]furo[3,4-e][1,4]diazepine-6-carboxylic acid 4b

Pale white solide Mp: 272–273 °C

IR(KBr): 3360, 3294, 1726, 1705, 1650, 1570, 1516, 1505, 1418, 1406, 1357, 1232, 1184, 1125, 1111, 1039, 1008, 827, cm^{-1}

^1H NMR (400 MHz, DMSO- d_6): 12.55 (s, 1H, COOH), 10.10 (s, 1H, NH), 7.58 (1H, d, $J = 1.6$ Hz, ArH), 7.41 (2H, d, $J = 8.4$ Hz, ArH), 7.30 (dd, $J = 1.6, 16.0$ Hz, 1H, ArH), 7.10 (d, $J = 8.4$ Hz, 2H, ArH) 6.71–6.69 (m, 2H, ArH and NH), 5.07 (d, $J = 4.4$ Hz, 1H, CH), 4.91 (s, 2H, CH_2)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{18}\text{H}_{14}\text{BrN}_2\text{O}_4$: 401.0132; found: 401.0105.

10-(2,4-Dichlorophenyl)-1-oxo-3,4,9,10-tetrahydro-1H-benzo[b]furo[3,4-e][1,4]diazepine-6-carboxylic acid 4c

Pale white solid, Mp: 285–287 °C

IR(KBr): 3379, 3322, 1724, 1692, 1660, 1571, 1511, 1463, 1392, 1358, 1198, 1167, 1137, 1046, 880, 855, 821, 756 cm^{-1}

^1H NMR (400 MHz, DMSO- d_6): 12.58 (s, 1H, COOH), 10.21 (s, 1H, NH), 7.61 (d, $J = 1.6$ Hz, 2H, ArH), 7.29 (dd, $J = 1.6, 16.8$ Hz, 1H, ArH), 7.17 (dd, $J = 2.0, 16.8$ Hz, 1H, ArH), 6.83 (d, $J = 8.4$ Hz, 1H, ArH), 6.72 (d, $J = 8.4$ Hz, 1H, ArH), 6.36 (d, $J = 4.4$ Hz, 1H, NH), 5.45 (d, $J = 4.4$ Hz, 1H, CH), 4.94 (s, 2H, CH_2)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{18}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}_4$: 391.0247; found: 391.0219.

10-(4-Nitrophenyl)-1-oxo-3,4,9,10-tetrahydro-1H-2-oxa-4,9-diazabenzof[*f*]azulene-6-carboxylic acid 4d

Pale white solid, Mp: >300 °C

IR(KBr): 3358, 3316, 3137, 1727, 1686, 1667, 1602, 1572, 1521, 1509, 1240, 1199, 1185, 1163, 1129, 1049, 1017, 820, cm^{-1}

^1H NMR (400 MHz, DMSO- d_6): 12.58 (s, 1H, COOH), 10.21 (s, 1H, NH), 8.10 (d, $J = 8.8$ Hz, 1H, ArH), 7.62 (s, 1H, ArH), 7.41 (d, $J = 8.8$ Hz, 2H, ArH), 7.31 (d, $J = 8.4$ Hz, 1H, ArH), 6.84 (d, $J = 4.4$ Hz, 1H, NH), 6.72 (d, $J = 8.4$ Hz, 1H, ArH), 5.21 (d, $J = 4.0$ Hz, 1H, CH), 4.94 (s, 2H, CH_2)

^{13}C NMR (100 MHz, DMSO- d_6 , 25 °C) (δ , ppm): 172.9, 167.3, 159.2, 151.7, 146.8, 141.3, 130.4, 128.6, 124.8, 124.0, 122.5, 122.5, 121.8, 96.0, 66.7, 57.0

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{18}\text{H}_{14}\text{N}_3\text{O}_6$: 368.0878; found: 368.0865.

1-Oxo-10-*p*-tolyl-3,4,9,10-tetrahydro-1H-2-oxa-4,9-diazabenzof[*f*]azulene-6-carboxylic acid 4e

Pale white solid, Mp: 278–280 °C

IR(KBr): 3361, 1724, 1702, 1650, 1570, 1513, 1359, 1186, 1170, 1123, 1039, 1008, 754 cm^{-1}

¹HNMR (400 MHz, DMSO-*d*₆): 12.49 (s, 1H, COOH), 10.02 (s, 1H, NH), 7.56 (s, 1H, ArH), 7.28 (d, *J* = 8.0 Hz, 1H, ArH), 7.02 (t, *J* = 8.4 Hz, 4H, ArH), 6.69 (d, *J* = 8.4 Hz, 1H, ArH), 6.65 (d, *J* = 4.0 Hz, 1H, NH), 5.05 (d, *J* = 4.0 Hz, 1H, CH), 4.90 (s, 2H, CH₂), 2.19 (s, 3H, CH₃)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ, ppm): 173.1, 167.3, 158.7, 142.2, 141.2, 136.3, 130.5, 129.2, 127.2, 124.6, 122.7, 122.4, 121.5, 97.3, 66.5, 57.1, 21.0

HRMS (ESI) *m/z*: calc. for [M+Na⁺] C₁₉H₁₆NaN₂O₄: 359.1003; found: 359.0991.

10-(4-Methoxyphenyl)-1-oxo-3,4,9,10-tetrahydro-1*H*-benzo[*b*]furo[3,4-*e*][1,4]diazepine-6-carboxylic acid 4f

Pale white solid, Mp: 251–253 °C

IR(KBr): 3361, 3079, 1724, 1651, 1570, 1511, 1410, 1347, 1252, 1177, 1114, 1038, 1008, 831, 760 cm⁻¹

¹HNMR (400 MHz, DMSO-*d*₆): 12.46 (s, 1H, COOH), 10.02 (s, 1H, NH), 7.55 (d, 1H, *J* = 1.6 Hz, ArH), 7.27 (dd, *J* = 1.6 Hz, 16.8 Hz, 1H, ArH), 7.05 (d, *J* = 8.8 Hz, 2H, ArH), 6.75 (d, *J* = 8.8 Hz, 1H, ArH), 6.68 (d, *J* = 8.4 Hz, 1H, ArH), 6.63 (d, *J* = 4.4 Hz, 1H, NH), 5.02 (d, *J* = 4.4 Hz, 1H, CH), 4.89 (s, 2H, CH₂), 3.65 (s, 3H, CH₃)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₉H₁₇N₂O₅: 353.1132; found: 353.1119.

10-(2,3-Dimethoxyphenyl)-1-oxo-3,4,9,10-tetrahydro-1*H*-benzo[*b*]furo[3,4-*e*][1,4]diazepine-6-carboxylic acid 4g

Pale white solid, Mp: >300 °C

IR(KBr): 3366, 3326, 3250, 3074, 2973, 1720, 1643, 1574, 1514, 1484, 1415, 1393, 1348, 1280, 1259, 1053, 1041, 1000, 852, cm⁻¹

¹HNMR (400 MHz, DMSO-*d*₆): 12.51 (s, 1H, COOH), 10.10 (s, 1H, NH), 7.60 (d, 1H, *J* = 1.6 Hz, ArH), 7.25 (dd, *J* = 2.0, 16.4 Hz, 1H, ArH), 6.86–6.83 (m, 1H, ArH), 6.77 (t, *J* = 8.0 Hz, 1H, ArH), 6.66 (d, *J* = 8.4 Hz, 1H, ArH), 6.26–6.24 (m, 1H, ArH), 6.12 (d, *J* = 4.4 Hz, 1H, NH), 5.42 (d, *J* = 4.4 Hz, 1H, CH), 4.91 (s, 2H, CH₂), 3.89 (s, 3H, CH₃), 3.78 (s, 3H, CH₃)

HRMS (ESI) *m/z*: calc. for [M+Na⁺] C₂₀H₁₈NaN₂O₆: 405.1058; found: 405.1073.

1-Oxo-10-thien-2-yl-3,4,9,10-tetrahydro-1*H*-2-oxa-4,9-diazabenzof[*f*]azulene-6-carboxylic acid 4h

Pale white solid, Mp: 285–286 °C

IR(KBr): 3336, 3305, 1720, 1696, 1652, 1572, 1508, 1404, 1353, 1267, 1227, 1144, 1043, 1007, 891, 828 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 12.56 (s, 1H, COOH), 10.07 (s, 1H, NH), 7.55 (d, *J* = 0.8 Hz, 1H, *Thienyl*-H), 7.35–7.33 (m, 1H, ArH), 7.26–7.25 (m, 1H, ArH), 6.85 (t, *J* = 4.0 Hz, 2H, *Thienyl*-H), 6.80 (d, *J* = 8.4 Hz, 1H, ArH), 6.77 (d, *J* = 4.8 Hz, 1H, NH), 5.30 (d, *J* = 4.4 Hz, 1H, CH), 4.88 (dd, *J* = 15.6, 17.8 Hz, 2H, CH₂)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₆H₁₂N₂NaO₄S: 351.0410; found: 351.0409.

10-Benzyl-1-oxo-3,4,9,10-tetrahydro-1H-2-oxa-4,9-diazabenzof[f]azulene-6-carboxylic acid 4i

Pale white solid, Mp: 249–250 °C

IR(KBr): 3524, 3350, 3299, 3132, 1688, 1637, 1573, 1516, 1497, 1422, 1353, 1277, 1252, 1231, 1190, 1129, 1047, 1027, 980 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 12.46 (s, 1H, COOH), 9.81 (s, 1H, NH), 7.51 (d, *J* = 1.6 Hz, 1H, ArH), 7.37 (dd, *J* = 2.0, 8.0 Hz, 1H, ArH), 7.24–7.21 (m, 2H, ArH), 7.18–7.14 (m, 1H, ArH), 7.03 (d, *J* = 7.2 Hz, ArH), 6.78 (1H, d, *J* = 8.4 Hz, ArH), 6.22 (1H, d, *J* = 4.4 Hz, 2H, NH), 4.80 (d, *J* = 15.2 Hz, CH₂), 4.69 (d, *J* = 15.2 Hz, CH₂), 4.15–4.11 (m, 1H, CH), 2.85–2.81 (m, 1H, CH₂), 2.71–2.65 (m, 1H, CH₂)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₉H₁₇N₂O₄: 337.1183; found: 337.1190.

7-Chloro-10-(4-chlorophenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[f]azulen-1-one 4j

Pale white solid, Mp: 250–252 °C

IR(KBr): 3345, 3273, 3140, 3095, 1715, 1666, 1621, 1563, 1499, 1420, 1398, 1363, 1186, 1057, 1031, 1014, 999, 872 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 10.00 (s, 1H, NH), 7.31–7.29 (m, 2H, ArH), 7.15–7.13 (m, 2H, ArH), 6.90 (d, *J* = 8.4 Hz, 1H, ArH), 6.80–6.78 (m, 1H, ArH), 6.68–6.67 (m, 1H, ArH), 6.36 (d, *J* = 4.4 Hz, 1H, NH), 5.05 (d, *J* = 4.0 Hz, 1H, CH), 4.90 (s, 2H, CH₂)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₇H₁₃Cl₂N₂O₂: 347.0349; found: 347.0343.

7-Chloro-10-(2,4-dichlorophenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[f]azulen-1-one 4k

Pale white solid, Mp: 272–274 °C

IR(KBr): 3387, 3274, 3088, 1722, 1710, 1628, 1569, 1501, 1464, 1411, 1354, 1331, 1237, 1184, 1103, 1046, 967, 868 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 10.13 (s, 1H, NH), 7.64 (d, *J* = 2.0 Hz, 1H, ArH), 7.19 (dd, *J* = 2.0, 8.4 Hz, 1H, ArH), 6.96 (d, *J* = 8.8 Hz, 1H, ArH), 6.84 (dd, *J* = 2.4, 8.6 Hz, 1H, ArH), 6.82 (d, *J* = 8.4 Hz, 1H, ArH), 6.72 (d, *J* = 2.4 Hz, 1H, ArH), 6.05 (d, *J* = 4.4 Hz, 1H, NH), 5.41 (d, *J* = 4 Hz, 1H, CH), 4.94 (s, 2H, CH₂)

HRMS (ESI) *m/z*: calc. for [M+Na⁺] C₁₇H₁₁Cl₃N₂NaO₂: 402.9779; found: 402.9796.

7-Chloro-10-*p*-tolyl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[f]azulen-1-one 4l

Pale white solid, Mp: 287–289 °C

IR(KBr): 3346, 3248, 3092, 1716, 1667, 1654, 1564, 1499, 1420, 1405, 1364, 1331, 1187, 1057, 1032, 998, 867 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 9.94 (s, 1H, NH), 7.04–6.99 (m, 4H, ArH), 6.88 (d, *J* = 8.4 Hz, 1H, ArH), 6.77–6.75 (m, 1H, ArH), 6.66 (s, 1H, ArH), 6.31 (d, *J* = 4.4 Hz, 1H, NH), 5.01 (d, *J* = 4.0 Hz, 1H, CH), 4.90 (s, 2H, CH₂), 2.21 (s, 3H, CH₃)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₈H₁₆ClN₂O₂: 327.0895; found: 327.0878.

7-Chloro-10-(2-methoxyphenyl)-3,4,9,10-tetrahydro-1H-benzo[b]furo[3,4-e][1,4]diazepin-1-one 4m

Pale white solid, Mp: 248–251 °C

IR(KBr): 3357, 3248, 3154, 1717, 1672, 1617, 1572, 1503, 1408, 1368, 1064, 1053, 1013, 1000, 777 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.96 (s, 1H, NH), 7.18–7.12 (m, 1H, ArH), 7.00 (d, J = 8.0 Hz, 1H, ArH), 6.87 (d, J = 8.4 Hz, 1H, ArH), 6.75 (dd, J = 8.4, 2.0 Hz, 1H, ArH), 6.68–6.60 (m, 3H, ArH), 5.75 (d, J = 4.4 Hz, 1H, NH), 5.34 (d, J = 4.4 Hz, 1H, CH), 4.98–4.89 (m, 2H, CH_2), 3.90 (s, 3H, CH_3).

HRMS (ESI) m/z : calc. for $[\text{M}+\text{Na}^+]$ $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{O}_3\text{Na}$ 365.0664; found: 365.0654.

7-Chloro-10-thien-2-yl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[f]azulen-1-one 4n

Pale yellow solid, Mp: 294–296 °C

IR(KBr): 3337, 3244, 3069, 1716, 1667, 1617, 1567, 1499, 1413, 1365, 1190, 1000, 868, 849, 808 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.99 (s, 1H, NH), 7.28–7.27 (m, 1H, ArH), 6.90–6.86 (m, 2H, ArH), 6.83–6.79 (m, 3H, *Thienyl*-H), 6.77–6.69 (m, 2H, ArH), 6.43 (d, J = 4.4 Hz, 1H, NH), 5.27 (d, J = 4.4 Hz, 1H, CH), 4.87 (dd, J = 15.6, 20.0 Hz, 2H, CH_2)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{15}\text{H}_{12}\text{ClN}_2\text{O}_2\text{S}$: 319.0303; found: 319.0290.

10-Benzyl-7-chloro-3,4,9,10-tetrahydro-2-oxa-4,9-diaza-benzof[f]azulen-1-one 4o

White solid, Mp: 234–235 °C

IR(KBr): 3379, 3276, 3107, 3027, 1721, 1637, 1569, 1496, 1490, 11417, 1362, 1339, 1190, 1037, 1028, 983 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.77 (s, 1H, NH), 7.27 (t, J = 7.2 Hz, 2H, ArH), 7.19 (t, J = 7.8 Hz, 1H, ArH), 7.06 (d, J = 7.2 Hz, 2H, ArH), 6.87 (d, J = 8.4 Hz, 1H, ArH), 6.82–6.78 (m, 2H, ArH), 5.87 (d, J = 4.4 Hz, 1H, NH), 4.77 (dd, J = 15.2, 20.2 Hz, 2H, CH_2), 4.11–4.06 (m, 1H, CH), 2.79–2.75 (m, 1H, CH_2), 2.68–2.63 (m, 1H, CH_2)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{18}\text{H}_{16}\text{ClN}_2\text{O}_2$: 327.0895; found: 327.0911.

6,7-Dichloro-10-(2,4-dichloro-phenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[f]azulen-1-one 4p

Pale white solid, Mp: 211–213 °C

IR(KBr): 3371, 3242, 3074, 1724, 1643, 1563, 1483, 1342, 1183, 1148, 1105, 1042, 1013, 879, 868 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 10.21 (s, 1H, NH), 7.64 (d, 1H, J = 2.0 Hz, ArH), 7.21 (dd, J = 2.0, 16.8 Hz, 1H, ArH), 7.13 (s, 1H, ArH), 6.91 (s, 1H, ArH), 6.83 (d, J = 8.4 Hz, 1H, ArH), 6.19 (d, J = 4.4 Hz, 1H, NH), 5.41 (d, J = 4.4 Hz, 1H, CH), 4.95 (dd, J = 15.6, 17.4 Hz, 2H, CH_2)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{17}\text{H}_{11}\text{Cl}_4\text{N}_2\text{O}_2$: 414.9570; found: 414.9551.

6,7-Dichloro-10-(4-nitro-phenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[*f*]azulen-1-one 4q

Pale yellow solid, Mp: 296–297 °C

IR(KBr): 3367, 3256, 3093, 1721, 1647, 1570, 1518, 1488, 1405, 1348, 1244, 1185, 1152, 1049, 1017, 875, 861 cm⁻¹

¹HNMR (400 MHz, DMSO-*d*₆): 10.21 (s, 1H, NH), 8.13 (d, *J* = 8.4 Hz, 2H, ArH), 7.40 (d, *J* = 8.8 Hz, 2H, ArH), 7.12 (s, 1H, ArH), 6.89 (s, 1H, ArH), 6.64 (d, *J* = 4.4 Hz, 1H, NH), 5.21 (d, *J* = 4.0 Hz, 1H, CH), 4.96 (dd, *J* = 15.6, 18.6 Hz, 2H, CH₂)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₇H₁₂Cl₂N₃O₄: 392.0200; found: 392.0178.

6,7-Dichloro-10-*p*-tolyl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[*f*]azulen-1-one 4r

Pale white solid, Mp: 282–284 °C

IR(KBr): 3350, 3286, 3093, 1724, 1646, 1566, 1487, 1403, 1344, 1328, 1242, 1183, 1149, 1044, 1008, 873 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 10.03 (s, 1H, NH), 7.05–6.98 (m, 5H, ArH), 6.83 (s, 1H, ArH), 6.44 (d, *J* = 4.4 Hz, 1H, NH), 5.01 (d, *J* = 4.4 Hz, 1H, CH), 4.91 (s, 2H, CH₂), 2.21 (s, 3H, CH₃)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₈H₁₅Cl₂N₂O₂: 361.0506; found: 361.0495.

6,7-Dichloro-10-thien-2-yl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[*f*]azulen-1-one 4s

Pale white solid, Mp: 261–263 °C

IR(KBr): 3335, 3247, 3096, 2943, 1718, 1665, 1639, 1561, 1487, 1407, 1342, 1255, 1227, 1177, 1143, 1039, 1006, 876 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 10.08 (s, 1H, NH), 7.29 (d, 1H, *J* = 5.2 Hz, *Thienyl*-H), 7.06 (s, 1H, ArH), 6.96 (s, 1H, ArH), 6.88 (m, 1H, *Thienyl*-H), 6.83 (d, *J* = 2.8 Hz, 1H, ArH), 6.55 (d, *J* = 4.4 Hz, 1H, NH), 5.28 (d, *J* = 4.4 Hz, 1H, CH), 4.89 (dd, *J* = 15.2, 23.6 Hz, 2H, CH₂)

HRMS (ESI) *m/z*: calc. for [M+Na⁺] C₁₅H₁₀Cl₂NaN₂O₂S: 374.9733; found: 374.9731.

10-Benzyl-6,7-dichloro-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[*f*]azulen-1-one 4t

White solid, Mp: 276–277 °C

IR(KBr): 3353, 3299, 3141, 3100, 3028, 1715, 1647, 1602, 1566, 1486, 1416, 1338, 1246, 1187, 1140, 1043, 1028, 987, 870 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 9.83 (s, 1H, NH), 7.27–7.23 (m, 2H, ArH), 7.20–7.17 (m, 1H, ArH), 7.05 (d, *J* = 7.2 Hz, 2H, ArH), 7.01 (s, 1H, ArH), 6.93 (s, 1H, ArH), 6.03 (d, *J* = 4.4 Hz, 1H, NH), 4.78 (dd, *J* = 15.2, 23.6 Hz, 2H, CH₂), 4.12–4.08 (m, 1H, CH), 2.82–2.77 (m, 1H, CH₂), 2.70–2.65 (m, 1H, CH₂)

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₈H₁₅Cl₂N₂O₂: 361.0506; found: 361.0491.

10-(4-Chlorophenyl)-3,4,9,10-tetrahydro-2-oxa-4,5,9-triazabenzof[*f*]azulen-1-one 4u

White solid, Mp: 262–264 °C

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1568, 1508, 1478, 1390, 1365, 1062, 1052, 1032, 1011 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.87 (s, 1H, NH), 7.25 (d, $J = 8.0$ Hz, 2H, ArH), 7.15 (d, $J = 8.4$ Hz, 2H, ArH), 6.90 (d, $J = 7.6$ Hz, 1H, ArH), 6.77–6.69 (m, 2H, ArH), 6.59 (d, $J = 7.2$ Hz, 1H, ArH), 6.09 (d, $J = 4.4$ Hz, 1H, NH), 5.06 (d, $J = 4.0$ Hz, 1H, CH), 4.90 (s, 2H, CH_2)

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 $^\circ\text{C}$) (δ , ppm): 173.2, 159.5, 143.1, 137.5, 132.1, 131.7, 129.4, 128.4, 123.5, 123.4, 121.4, 120.1, 96.7, 66.6, 57.2

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{17}\text{H}_{14}\text{ClN}_2\text{O}_2$: 313.0739; found: 313.0712.

10-(4-Bromophenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4v

White solid, Mp: >300 $^\circ\text{C}$

IR(KBr): 3352, 3247, 3150, 3104, 1716, 1670, 1617, 1595, 1568, 1508, 1478, 1454, 1403, 1390, 1365, 1334, 1062, 1052, 774, cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.88 (s, 1H, NH), 7.39 (d, $J = 8.0$ Hz, 2H, ArH), 7.09 (d, $J = 8.4$ Hz, 2H, ArH), 6.90 (d, $J = 7.6$ Hz, 1H, ArH), 6.77–6.69 (m, 2H, ArH), 6.59 (d, $J = 7.6$ Hz, 1H, ArH), 6.09 (d, $J = 4.4$ Hz, 1H, NH), 5.04 (d, $J = 4.0$ Hz, 1H, CH), 4.90 (s, 2H, CH_2)

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 $^\circ\text{C}$) (δ , ppm): 173.2, 159.5, 143.6, 137.5, 132.1, 131.3, 129.8, 123.5, 123.4, 121.4, 120.2, 120.1, 96.7, 66.6, 57.3

HRMS (ESI) m/z : calc. for $[\text{M}+\text{Na}^+]$ $\text{C}_{17}\text{H}_{13}\text{BrNaN}_2\text{O}_2$: 379.0053; found: 379.0037.

10-(2,4-Dichlorophenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4w

White solid, Mp: 204–205 $^\circ\text{C}$

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1568, 1508, 1478, 1403, 1390, 1365, 1334, 1062, 1032, 774, cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 10.00 (s, 1H, NH), 7.60 (s, 1H, ArH), 7.14 (d, $J = 8.0$ Hz, 1H, ArH), 6.96 (d, $J = 8$ Hz, 1H, ArH), 6.81 (m, 2H, ArH), 6.71 (t, $J = 7.6$ Hz, 1H, ArH), 6.58 (d, $J = 7.6$ Hz, 1H, ArH), 5.71 (d, $J = 4.0$ Hz, 1H, NH), 5.41 (d, $J = 4.4$ Hz, 1H, CH), 4.94 (s, 2H, CH_2)

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 $^\circ\text{C}$) (δ , ppm): 172.7, 160.4, 139.6, 136.6, 134.6, 132.7, 132.7, 129.3, 129.3, 127.2, 123.8, 122.2, 120.1, 96.0, 66.8, 54.8

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{17}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}_2$: 347.0349; found: 347.0347.

10-(4-Nitrophenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4x

Yellow solid, Mp: 219–220 $^\circ\text{C}$

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1568, 1508, 1478, 1403, 1390, 1365, 1334, 1062, 1032, 774, cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.99 (s, 1H, NH), 8.08 (d, $J = 8.0$ Hz, 2H, ArH), 7.40 (d, $J = 8.4$ Hz, 2H, ArH), 6.94 (d, $J = 7.6$ Hz, 1H, ArH), 6.78 (t, $J = 7.2$ Hz, 1H, ArH), 6.72 (d, J

= 7.2 Hz, 1H, ArH), 6.61 (d, J = 7.6 Hz, 1H, ArH), 6.26 (d, J = 4.4 Hz, 1H, NH), 5.18 (d, J = 4.4 Hz, 1H, CH), 4.94 (s, 2H, CH₂)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ , ppm): 173.1, 159.7, 151.8, 146.7, 137.1, 132.0, 128.7, 123.7, 123.7, 123.3, 121.7, 120.3, 96.0, 66.7, 57.4

HRMS (ESI) m/z : calc. for [M+H⁺] C₁₇H₁₄N₃O₄: 324.0979; found: 324.0956.

10-(2-Chlorophenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofluzulen-1-one 4y

White solid, Mp: 233–235 °C

IR(KBr): 3395, 3156, 3063, 2989, 2952, 2930, 2899, 1725, 1652, 1574, 1506, 1484, 1444, 1398, 1363, 1233, 1122, 1046, 985, cm⁻¹

¹HNMR (400 MHz, DMSO-*d*₆): 9.98 (s, 1H, NH), 7.43 (d, J = 4.0 Hz, 1H, ArH), 7.16 (t, J = 7.2 Hz, 1H, ArH), 7.03 (t, J = 7.6 Hz, 1H, ArH), 6.96 (d, J = 7.6 Hz, 1H, ArH), 6.79 (t, J = 7.6 Hz, 2H, ArH), 6.68 (t, J = 7.2 Hz, 1H, ArH), 6.56 (d, J = 7.6 Hz, 1H, ArH), 5.63 (d, J = 4.4 Hz, 1H, NH), 5.47 (d, J = 4.4 Hz, 1H, CH), 4.95 (s, 2H, CH₂)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ , ppm): 172.8, 160.4, 140.4, 136.7, 133.7, 132.6, 130.0, 129.2, 128.0, 127.1, 123.7, 123.6, 122.0, 120.0, 96.4, 66.7, 55.3

HRMS (ESI) m/z : calc. for [M+H⁺] C₁₇H₁₄ClN₂O₂: 313.0739; found: 313.0724.

10-(3-Nitrophenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofluzulen-1-one 4z

Yellow solid, Mp: 252–255 °C

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1568, 1478, 1454, 1438, 1403, 1365, 1062, 1032, 1011, 774, cm⁻¹

¹HNMR (400 MHz, DMSO-*d*₆): 9.97 (s, 1H, NH), 8.09 (s, 1H, ArH), 8.00 (d, J = 8.0 Hz, 1H, ArH), 7.55–7.47 (m, 2H, ArH), 6.94 (d, J = 7.6 Hz, 1H, ArH), 6.79–6.70 (m, 2H, ArH), 6.62 (d, J = 8.0 Hz, 1H, ArH), 6.25 (d, J = 4.4 Hz, 1H, NH), 5.22 (d, 1H, J = 4 Hz, CH), 4.95 (s, 2H, CH₂)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ , ppm): 173.2, 159.9, 148.1, 146.4, 137.1, 133.9, 132.2, 130.0, 123.7, 123.4, 122.4, 122.2, 121.8, 120.3, 96.1, 66.7, 57.4

HRMS (ESI) m/z : calc. for [M+H⁺] C₁₇H₁₄N₃O₄: 324.0979; found: 324.0957.

4-(1-Oxo-3,4,9,10-tetrahydro-1H-2-oxa-4,9-diazabenzofluzulen-10-yl)-benzonitrile 4aa

Pale white solid, Mp: 279–281 °C

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1508, 1478, 1454, 1438, 1390, 1365, 1334, 1062, 1032, 774, cm⁻¹

¹HNMR (400 MHz, DMSO-*d*₆): 9.96 (s, 1H, NH), 7.68 (d, J = 8.4 Hz, 2H, ArH), 7.32 (d, J = 8.0 Hz, 2H, ArH), 6.93 (d, J = 7.2 Hz, 1H, ArH), 6.79–6.70 (m, 2H, ArH), 6.59 (d, J = 7.6 Hz, 1H, ArH), 6.22 (d, J = 4.0 Hz, 1H, NH), 5.12 (d, J = 4 Hz, 1H, CH), 4.92 (s, 2H, CH₂)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ , ppm): 173.1, 159.7, 149.7, 137.2, 132.5, 132.0, 128.5, 123.6, 123.3, 121.6, 120.2, 119.2, 109.9, 96.0, 66.7, 57.6

HRMS (ESI) m/z : calc. for $[M+H]^+$ $C_{18}H_{14}N_3O_2$: 304.1081; found: 304.1071.

10-Phenyl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4bb

White solid, Mp: 290–291 °C

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1568, 1508, 1478, 11403, 1390, 1334, 1062, 1052, 1011, 774, cm^{-1} .

1H NMR(400 MHz, DMSO- d_6): 9.83 (s, 1H, NH), 7.20–7.09 (m, 5H, ArH), 6.89 (d, J = 7.8 Hz, 1H, ArH), 6.75–6.66 (m, 2H, ArH), 6.59 (d, J = 6.8 Hz, 1H, ArH), 6.07 (d, J = 4.4 Hz, 1H, NH), 5.05 (d, J = 4.4 Hz, 1H, CH), 4.90 (s, 2H, CH₂)

^{13}C NMR (100 MHz, DMSO- d_6 , 25 °C) (δ , ppm): 173.3, 159.2, 144.2, 137.8, 131.9, 128.4, 127.5, 127.0, 123.3, 123.3, 121.1, 120.0, 97.2, 66.5, 57.8

HRMS (ESI) m/z : calc. for $[M+H]^+$ $C_{17}H_{15}N_2O_2$: 279.1129; found: 279.1127.

10-*p*-Tolyl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4cc

White solid, Mp: 287–288 °C

IR(KBr): 3351, 3246, 3202, 3149, 3102, 3083, 2965, 1717, 1645, 1639, 1568, 1509, 1487, 1387, 1197, 1061, 1033, 995, 851, 845 cm^{-1} .

1H NMR (400 MHz, DMSO- d_6): 9.81 (s, 1H, NH), 7.00 (dd, J = 8.0, 14.4 Hz, 4H, ArH), 6.89 (d, J = 7.6 Hz, 1H, ArH), 6.74–6.66 (m, 2H, ArH), 6.58 (d, J = 7.2 Hz, 1H, ArH), 6.03 (d, J = 4.0 Hz, 1H, NH), 5.02 (d, J = 4.0 Hz, 1H, CH), 4.89 (s, 2H, CH₂), 2.18 (s, 3H, CH₃)

^{13}C NMR (100 MHz, DMSO- d_6 , 25 °C) (δ , ppm): 173.2, 159.5, 143.6, 137.5, 132.1, 131.3, 129.8, 123.5, 123.4, 121.4, 120.2, 120.1, 96.7, 66.6, 57.3

HRMS (ESI) m/z : calc. for $[M+H]^+$ $C_{18}H_{17}N_2O_2$: 293.1285; found: 293.1279.

10-(2-Methoxyphenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4dd

White solid, Mp: 247–259 °C

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1568, 1508, 1478, 1438, 1403, 1390, 1062, 1052, 1032, 1011, 774 cm^{-1} .

1H NMR (400 MHz, DMSO- d_6): 9.88 (s, 1H, NH), 7.39 (d, J = 8.0 Hz, 2H, ArH), 7.09 (d, J = 8.4 Hz, 2H, ArH), 6.90 (d, J = 7.6 Hz, 1H, ArH), 6.77–6.69 (m, 2H, ArH), 6.59 (d, J = 7.6 Hz, 1H, ArH), 6.09 (d, J = 4.4 Hz, 1H, NH), 5.04 (d, J = 4.0 Hz, 1H, CH), 4.90 (s, 2H, CH₂)

^{13}C NMR (100 MHz, DMSO- d_6 , 25 °C) (δ , ppm): 173.2, 159.5, 143.6, 137.5, 132.1, 131.3, 129.8, 123.5, 123.4, 121.4, 120.2, 120.1, 96.7, 66.6, 57.3

HRMS (ESI) m/z : calc. for $[M+H]^+$ $C_{18}H_{17}N_2O_3$: 309.1234; found: 309.1220.

10-(3,4,5-Trimethoxyphenyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4ee

Pale white solid, Mp: 259–260 °C

IR(KBr): 3323, 3301, 3105, 2994, 2945, 2832, 1716, 1661, 1627, 1603, 1565, 1485, 1418, 1390, 1305, 1252, 1153, 1047, 783, cm^{-1} .

¹HNMR (400 MHz, DMSO-*d*₆): 9.83 (s, 1H, NH), 6.91–6.89 (m, 1H, ArH), 6.78–6.71 (m, 2H, ArH), 6.67–6.64 (m, 1H, ArH), 6.41 (s, 2H, ArH), 6.01 (d, *J* = 4.4 Hz, 1H, NH), 4.97 (d, *J* = 4.0 Hz, 1H, CH), 4.90 (d, *J* = 15.6 Hz, 1H, CH₂), 4.86 (d, *J* = 15.6 Hz, 1H, CH₂), 3.58 (s, 6H, CH₃), 3.55 (s, 3H, CH₃)

HRMS (ESI) *m/z*: calc. for [M+Na⁺] C₂₀H₂₀NaN₂O₅: 391.1265; found: 391.1262.

10-(4-Dimethylaminophenyl)-3,4,9,10-tetrahydro-2-oxa-4,5,9-triazabenzof[f]azulen-1-one 4ff

Pale white solid, Mp: 273–276 °C

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1568, 1508, 1454, 1438, 1390, 1365, 1334, 1062, 1011, 774, cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 9.74 (s, 1H, NH), 6.94 (d, *J* = 8.4 Hz, 2H, ArH), 6.87 (d, *J* = 7.2 Hz, 1H, ArH), 6.73–6.66 (m, 2H, ArH), 6.60 (d, *J* = 7.2 Hz, 1H, ArH), 6.53 (d, *J* = 8.8 Hz, 2H, ArH), 5.94 (d, *J* = 4.4 Hz, 1H, NH), 4.96 (d, *J* = 4.0 Hz, 1H, CH), 4.87 (s, 2H, CH₂), 2.79 (s, 6H, CH₃)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ, ppm): 173.4, 158.9, 149.6, 138.2, 132.0, 128.2, 123.3, 123.2, 119.8, 112.4, 197.9, 66.4, 57.2

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₉H₂₀N₃O₂: 322.1551; found: 322.1551.

10-Thien-2-yl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[f]azulen-1-one 4gg

Pale yellow solid, Mp: 282–283 °C

IR(KBr): 3352, 3247, 3150, 3104, 3083, 1716, 1670, 1617, 1595, 1508, 1478, 1454, 1403, 1390, 1365, 1062, 1052, 1032, 774 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 9.88 (1H, s, NH), 7.39 (d, *J* = 8.0 Hz, 2H, ArH), 7.09 (d, *J* = 8.4 Hz, 2H, ArH), 6.90 (d, *J* = 7.6 Hz, 1H, ArH), 6.77–6.69 (m, 2H, ArH), 6.59 (d, *J* = 7.6 Hz, 1H, ArH), 6.09 (d, *J* = 4.4 Hz, 1H, NH), 5.04 (d, *J* = 4.0 Hz, 1H, CH), 4.90 (s, 2H, CH₂)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ, ppm): 173.0, 159.1, 148.6, 137.6, 132.1, 127.0, 125.1, 123.7, 123.5, 121.6, 120.1, 98.2, 66.5, 53.3

HRMS (ESI) *m/z*: calc. for [M+Na⁺] C₁₅H₁₂N₂NaO₂S: 307.0512; found: 307.0513.

10-Benzyl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzof[f]azulen-1-one 4hh

White solid, Mp: 229–231 °C

IR(KBr): 3349, 3287, 3154, 3101, 1720, 1640, 1568, 1507, 1489, 1438, 1396, 1335, 1192, 1047, 766, 747, 702 cm⁻¹.

¹HNMR (400 MHz, DMSO-*d*₆): 9.66 (s, 1H, NH), 7.28 (t, *J* = 7.4 Hz, 2H, ArH), 7.20 (t, *J* = 7.2 Hz, 1H, ArH), 7.09 (d, *J* = 7.2 Hz, 2H, ArH), 6.90 (d, *J* = 7.2 Hz, 1H, ArH), 6.86–6.78 (m, 2H, ArH), 6.72 (d, *J* = 7.2 Hz, 1H, ArH), 5.43 (d, *J* = 4.0 Hz, 1H, NH), 4.76 (dd, *J* = 15.2, 4.0 Hz, 2H, CH₂), 2.78–2.73 (m, 1H, CH₂), 2.64–2.58 (m, 1H, CH₂)

¹³CNMR (100 MHz, DMSO-*d*₆, 25 °C) (δ, ppm): 173.1, 158.5, 139.1, 137.3, 131.8, 129.8, 128.7, 126.6, 123.7, 123.2, 121.0, 120.1, 98.6, 66.5, 55.7, 44.3

HRMS (ESI) *m/z*: calc. for [M+H⁺] C₁₈H₁₇N₂O₂: 293.1285; found: 293.1287.

10-Isobutyl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4ii

White solid, Mp: 208–210 °C

IR(KBr): 3346, 2952, 2926, 1737, 1666, 1560, 1502, 1475, 1390, 1363, 1337, 1186, 1030, 1011, 969, 758, 647 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.64 (s, 1H, NH), 6.88 (d, $J = 7.2$ Hz, 2H, ArH), 6.83–6.76 (m, 2H, ArH), 5.69 (d, $J = 4.4$ Hz, 1H, NH), 4.77 (dd, $J = 15.2, 18.8$ Hz, 2H, CH_2), 3.92–3.87 (m, 1H, CH), 1.72–1.65 (m, 1H, CH), 1.28–1.22 (m, 1H, CH_2), 1.12–1.05 (m, 1H, CH_2), 0.88 (d, $J = 6.4$ Hz, 3H, CH_3), 0.83 (d, $J = 6.4$ Hz, 3H, CH_3)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{Na}^+]$ $\text{C}_{15}\text{H}_{18}\text{NaN}_2\text{O}_2$: 281.1261; found: 281.1274.

10-sec-Butyl-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4jj

White solid, Mp: 173–175 °C

IR(KBr): 3355, 3293, 3109, 2963, 2929, 2874, 1731, 1651, 1567, 1490, 1437, 1393, 1359, 1335, 1186, 1151, 1122, 1043, 772 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.65 (s, 1H, NH), 6.90–6.84 (m, 2H, ArH), 6.82–6.78 (m, 1H, ArH), 6.75–6.72 (m, 1H, ArH), 5.83–5.80 (m, 1H, NH), 4.77 (s, 2H, CH_2), 3.92–3.87 (m, 1H, CH), 3.60–3.54 (m, 1H, CH), 1.56–1.26 (m, 2H, CH_2), 1.17–0.94 (m, 1H, CH), 0.81–0.72 (m, 6H, CH_3)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{Na}^+]$ $\text{C}_{15}\text{H}_{18}\text{N}_2\text{NaO}_2$: 281.1261; found: 281.1276.

10-(1-Methylbutyl)-3,4,9,10-tetrahydro-2-oxa-4,9-diazabenzofazulen-1-one 4kk

White solid, Mp: 173–174 °C

IR(KBr): 3352, 2963, 2930, 2871, 1731, 1651, 1566, 1488, 1436, 1393, 1360, 1333, 1186, 1153, 1042, 1030, 986, 772, 756 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.66 (s, 1H, NH), 6.91–6.85 (m, 2H, ArH), 6.82–6.79 (m, 1H, ArH), 6.77–6.73 (m, 1H, ArH), 5.82 (d, 1H, $J = 4.8$ Hz, NH), 4.76 (m, 2H, CH_2), 3.56–3.53 (m, 1H, CH), 1.51–1.26 (m, 3H, CH and CH_2), 1.13–0.96 (m, 2H, CH_2), 0.80–0.71 (m, 6H, CH_3)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{Na}^+]$ $\text{C}_{16}\text{H}_{20}\text{N}_2\text{NaO}_2$: 295.1417; found: 295.1410.

10-Cyclohexyl-3,4,9,10-tetrahydro-2-oxa-4,9-diaza-benzo[f]azulen-1-one 4ll

White solid, Mp: 256–257 °C

IR(KBr): 3483, 3350, 3325, 3058, 2934, 2853, 1731, 1706, 1654, 1616, 1565, 1508, 1486, 1434, 1393, 1191, 1178, 1041, 801 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.64 (s, 1H, NH), 6.89–6.84 (m, 2H, ArH), 6.80 (t, $J = 7.6$ Hz, 1H, ArH), 6.76–6.72 (m, 1H, ArH), 5.83 (d, $J = 4.8$ Hz, 1H, NH), 4.78 (d, $J = 15.2$ Hz, 1H, CH_2), 4.73 (d, $J = 15.2$ Hz, 1H, CH_2), 3.49 (dd, $J = 4.8, 15.2$ Hz, 1H, CH), 1.85–1.84 (m, 1H, CH), 1.62–1.39 (m, 4H, CH_2), 1.15–0.98 (m, 4H, CH_2), 0.94–0.87 (m, 2H, CH_2)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{H}^+]$ $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_2$: 285.1598; found: 285.1595.

10-Isopropyl-3,4,9,10-tetrahydro-2-oxa-4,9-diaza-benzo[*f*]azulen-1-one 4mm

White solid, Mp: 254–256 °C

IR(KBr): 3469, 3329, 3276, 3152, 3101, 2960, 1708, 1652, 1570, 1508, 1479, 1435, 1395, 1364, 1333, 1232, 1045, 998, 849 cm^{-1} .

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.66 (s, 1H, NH), 6.91–6.85 (m, 2H, ArH), 6.82–6.79 (m, 1H, ArH), 6.77–6.73 (m, 1H, ArH), 5.82 (d, $J = 4.8$ Hz, 1H, NH), 4.77 (s, 2H, CH_2), 3.46 (dd, $J = 4.8, 8.4$ Hz, 1H, CH), 1.53–1.44 (m, 1H, CH), 0.86 (d, $J = 6.4$ Hz, 3H, CH_3), 0.82 (d, $J = 6.8$ Hz, 3H, CH_3)

HRMS (ESI) m/z : calc. for $[\text{M}+\text{Na}^+]$ $\text{C}_{14}\text{H}_{17}\text{N}_2\text{O}_2$: 245.1285; found: 245.1289.

General procedure for the synthesis of products 5a

In a 10-mL reaction vial, the benzene-1,2-diamine **1a** (1 mmol), tetronic acid **3** (1 mmol), acetic acid (0.1 mmol) and water (2 mL) were mixed and then stirring for 10 min. Subsequently, the 2-formylbenzoic acids **2** (1 mmol) was added to the reaction mixture, and the reaction vial was capped and pre-stirring for 20 second. The mixture was subjected to microwave irradiation at 200W (initial power 100W, maximum power 200W) at 150 °C, for 15 min. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature, filtered to give the crude product, which was further washed by 50% EtOH to give pure product **5a**.

4bH-Benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-5,14(7H,8H)-dione 5a

White solid, MP: 286–289 °C

IR(KBr): 3277, 3220, 3147, 3108, 1734, 1704, 1688, 1730, 1595, 1543, 1506, 1397, 1348, 1194, 1045, 1023, 766 cm^{-1}

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.99(s, 1H, NH), 8.41 (d, 1H, $J = 8.0$ Hz, ArH), 7.78 (d, 1H, $J = 7.6$ Hz, ArH), 7.70–7.66 (m, 1H, ArH), 7.59–7.55 (m, 1H, ArH), 7.40–7.34 (m, 2H, ArH), 7.21–7.14 (m, 2H, ArH), 5.74 (s, 1H, CH), 4.83 (d, $J = 15.2$ Hz, 1H, CH_2), 4.78 (d, $J = 15.2$ Hz, 1H, CH_2)

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 °C) (δ , ppm): 171.8, 165.8, 158.5, 143.9, 136.8, 131.6, 130.7, 130.6, 128.8, 128.2, 126.3, 123.3, 123.1, 119.4, 94.4, 66.6, 59.3.

HRMS (ESI) m/z : calc. for $[\text{M}-\text{H}^+]$ $\text{C}_{18}\text{H}_{11}\text{N}_2\text{O}_3$: 303.0764; found: 303.0761.

1,2-Dimethoxy-4bH-benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-5,14(7H,8H)-dione 5b

White solid, Mp: 291–293 °C

IR(KBr): 3251, 3201, 3141, 3092, 1752, 1677, 1655, 1596, 1557, 1497, 1376, 1337, 1272, 1062, 1040, 1011, 773 cm^{-1}

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 9.93 (s, 1H, NH), 8.06 (d, 1H, $J = 8.4$ Hz, ArH), 7.37–7.32 (m, 3H, ArH), 7.19–7.13 (m, 2H, ArH), 5.58 (s, 1H, CH), 4.87 (d, $J = 15.2$ Hz, CH_2), 4.83 (d, $J = 15.2$ Hz, CH_2), 4.87 (d, $J = 15.2$ Hz, 1H, CH_2), 4.85 (d, $J = 15.2$ Hz, 1H, CH_2), 3.85 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3)

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 °C) (δ , ppm): 171.8, 163.9, 158.3, 152.4, 146.3, 137.1, 136.8, 130.9, 128.1, 126.4, 123.0, 121.6, 119.4, 116.8, 95.1, 66.5, 61.6, 58.0, 56.4.

HRMS (ESI) m/z : calc. for $[M-H^+]$ $C_{20}H_{15}N_2O_5$: 363.0975; found: 363.0976.

10,11-Dimethyl-4bH-benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-5,14(7H,8H)-dione 5c

White solid, Mp: >300 °C

IR(KBr): 3270, 3186, 3124, 3082, 1753, 1687, 1653, 1614, 1510, 1398, 1362, 1340, 1211, 1195, 1141, 1115, 1065, 1024, 760 cm^{-1}

1H NMR (400 MHz, DMSO- d_6): 9.94 (s, 1H, NH), 8.40 (d, 1H, $J = 7.6$ Hz, ArH), 7.75 (d, 1H, $J = 7.2$ Hz, ArH), 7.67 (t, 1H, $J = 7.6$ Hz, ArH), 7.58–7.54 (m, 1H, ArH), 7.14 (s, 1H, ArH), 6.95 (s, 1H, ArH), 5.67 (s, 1H, CH), 4.84 (d, $J = 15.2$ Hz, 1H, CH_2), 4.74 (d, $J = 15.2$ Hz, 1H, CH_2), 2.24 (s, 3H, CH_3), 2.20 (s, 3H, CH_3)

HRMS (ESI) m/z : calc. for $[M-H^+]$ $C_{20}H_{15}N_2O_3$: 331.1077; found: 331.1075.

1,2-Dimethoxy-10,11-dimethyl-4bH-benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-5,14(7H,8H)-dione 5d

White solid, Mp: >300 °C

IR(KBr): 3255, 3196, 3127, 3088, 3001, 1749, 1682, 1667, 1620, 1557, 1448, 1400, 1270, 1197, 1117, 1060, 1015, 958 cm^{-1}

1H NMR (400 MHz, DMSO- d_6): 9.77 (s, 1H, NH), 8.05 (d, $J = 8.4$ Hz, 1H, ArH), 7.34 (d, $J = 8.4$ Hz, 1H, ArH), 7.11 (s, 1H, ArH), 6.93 (s, 1H, ArH), 5.51 (s, 1H, CH), 4.83 (d, $J = 15.2$ Hz, 1H, CH_2), 4.72 (d, $J = 15.2$ Hz, 1H, CH_2), 3.84 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 2.23 (s, 3H, CH_3), 2.20 (s, 3H, CH_3)

^{13}C NMR (100 MHz, DMSO- d_6 , 25 °C) (δ , ppm): 171.9, 163.9, 158.4, 152.3, 146.2, 138.8, 136.4, 134.5, 131.1, 131.0, 123.8, 123.0, 121.6, 120.0, 116.6, 94.4, 66.4, 61.6, 58.0, 56.4, 19.1, 18.5.

HRMS (ESI) m/z : calc. for $[M-H^+]$ $C_{22}H_{19}N_2O_5$: 391.1288; found: 391.1284.

10,11-Dichloro-4bH-benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-5,14(7H,8H)-dione 5e

Pale white solid, Mp: >300 °C

IR(KBr): 3330, 3281, 3134, 3102, 1747, 1715, 1662, 1626, 1597, 1557, 1487, 1408, 1259, 1179, 1135, 1014, 871 cm^{-1}

1H NMR (400 MHz, DMSO- d_6): 10.18 (s, 1H, NH), 8.41 (d, $J = 7.6$ Hz, 1H, ArH), 7.80 (d, $J = 7.6$ Hz, 1H, ArH), 7.73–7.69 (m, 2H, ArH), 7.61–7.57 (m, 1H, ArH), 7.39 (s, 1H, ArH), 5.76 (s, 1H, CH), 4.91 (d, $J = 15.2$ Hz, 1H, CH_2), 4.79 (d, $J = 15.2$ Hz, 1H, CH_2)

^{13}C NMR (100 MHz, DMSO- d_6 , 25 °C) (δ , ppm): 171.6, 165.9, 157.8, 143.7, 137.1, 132.1, 132.0, 130.2, 130.5, 129.0, 126.3, 124.0, 123.5, 120.4, 112.7, 95.6, 66.6, 59.0.

HRMS (ESI) m/z : calc. for $[M-H^+]$ $C_{18}H_9Cl_2N_2O_3$: 370.9984; found: 370.9982.

10,11-Dichloro-1,2-dimethoxy-4bH-benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-5,14(7H,8H)-dione 5f

Pale white solid, Mp: 263–265 °C

IR(KBr): 3249, 1747, 1681, 1672, 1592, 1537, 1489, 1474, 1393, 1342, 1194, 1134, 1111, 1055, 1027, 742 cm^{-1}

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 10.10 (s, 1H, NH), 8.06 (d, $J = 8.4$ Hz, 1H, ArH), 7.68 (s, 1H, ArH), 7.39–7.37 (m, 2H, ArH), 5.59 (s, 1H, CH), 4.90 (d, $J = 15.2$ Hz, 1H, CH_2), 4.76 (d, $J = 15.2$ Hz, 1H, CH_2), 3.85 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3).

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 $^\circ\text{C}$) (δ , ppm): 171.5, 163.9, 157.6, 152.4, 146.4, 137.3, 136.5, 132.3, 129.9, 126.1, 123.9, 122.5, 121.6, 120.3, 117.2, 96.2, 66.6, 61.6, 57.6, 56.4.

HRMS (ESI) m/z : calc. for $[\text{M}-\text{H}^+]$ $\text{C}_{20}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}_5$: 432.0196; found: 432.0199.

5,14-Dioxo-5,7,8,14-tetrahydro-4bH-benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-10-carboxylic acid 5g

Pale white solid, MP: >300 $^\circ\text{C}$

IR(KBr): 3340, 3116, 1748, 1701, 1687, 1616, 1562, 1516, 1404, 1390, 1342, 1268, 1314, 1182, 1058, 1023, 771 cm^{-1}

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 13.21 (s, 1H, COOH), 10.17 (s, 1H, NH), 8.43 (d, 1H, $J = 7.6$ Hz, ArH), 7.83 (d, 1H, $J = 2.0$ Hz, ArH), 7.80 (d, 1H, $J = 7.6$ Hz, ArH), 7.73–7.68 (m, 2H, ArH), 7.61–7.57 (m, 1H, ArH), 7.52 (d, 1H, $J = 8.0$ Hz, ArH), 5.80 (s, 1H, CH), 4.90 (d, $J = 15.2$ Hz, 1H, CH_2), 4.81 (d, $J = 15.2$ Hz, 1H, CH_2).

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 $^\circ\text{C}$) (δ , ppm): 171.6, 166.4, 165.9, 158.3, 143.9, 136.7, 135.9, 131.9, 131.0, 130.4, 130.3, 130.0, 128.9, 126.4, 123.4, 120.5, 94.7, 66.5, 59.2.

HRMS (ESI) m/z : calc. for $[\text{M}-\text{H}^+]$ $\text{C}_{19}\text{H}_{11}\text{N}_2\text{O}_5$: 347.0662; found: 347.0659.

1,2-Dimethoxy-5,14-dioxo-5,7,8,14-tetrahydro-4bH-benzo[2,3]furo[3',4':5,6][1,4]diazepino[7,1-a]isoindole-10-carboxylic acid 5h

Pale white solid, Mp: 277–280 $^\circ\text{C}$

IR(KBr): 3313, 3138, 1750, 1689, 1672, 1558, 1499, 1400, 1275, 1061, 1047, 783, 774, 755 cm^{-1}

^1H NMR (400 MHz, $\text{DMSO}-d_6$): 13.18 (s, 1H, COOH), 10.11 (s, 1H, NH), 8.08 (d, 1H, $J = 8.4$ Hz, ArH), 7.81 (s, 1H, ArH), 7.68–7.66 (m, 1H, ArH), 7.51–7.49 (m, 1H, ArH), 7.38 (d, 1H, $J = 8.4$ Hz, ArH), 5.62 (s, 1H, CH), 4.89 (d, $J = 15.2$ Hz, 1H, CH_2), 4.78 (d, $J = 15.2$ Hz, 1H, CH_2), 3.85 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3).

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 25 $^\circ\text{C}$) (δ , ppm): 171.7, 166.4, 163.9, 158.1, 152.4, 146.4, 136.9, 136.7, 131.1, 130.3, 130.1, 123.3, 122.8, 121.7, 120.5, 117.0, 95.2, 66.5, 61.6, 57.8, 56.4.

HRMS (ESI) m/z : calc. for $[\text{M}-\text{H}^+]$ $\text{C}_{21}\text{H}_{15}\text{N}_2\text{O}_7$: 407.0874; found: 407.0880.

Crystal data for **4g**: $\text{C}_{26}\text{H}_{32}\text{N}_4\text{O}_8$, pale white, crystal dimension $0.40 \times 0.35 \times 0.14$ mm, Monoclinic, space group $\text{P2}(1)/c$, $a = 11.9237(11)$ Å, $b = 14.1491(13)$ Å, $c = 16.7626(14)$ Å, $\alpha = \gamma = 90$ $^\circ$, $\beta = 99.5980(10)$ $^\circ$, $V = 2788.4(4)$ Å³, $Mr = 528.56$, $Z = 4$, $D_c = 1.259$ Mg/m³, $\lambda = 0.71073$ Å, $\mu(\text{Mo K}\alpha) = 0.094$ mm⁻¹, $F(000) = 1120$, $R = 0.0552$, $wR_2 = 0.1182$, $S = 1.036$, largest diff. Peak and hole: 0.508 and -0.324 e/Å³. CCDC-823409 contains the supplementary crystallographic data for this paper

Crystal data for **4u**: $C_{17}H_{13}BrN_2O_2$, pale white, crystal dimension $0.35 \times 0.20 \times 0.11$ mm, Monoclinic, space group $P2(1)/c$, $a = 14.6324(15)$ Å, $b = 12.0632(12)$ Å, $c = 8.5627(9)$ Å, $\alpha = \gamma = 90^\circ$, $\beta = 94.7470(10)^\circ$, $V = 1506.2(3)$ Å³, $Mr = 357.20$, $Z = 4$, $D_c = 1.575$ Mg/m³, $\lambda = 0.71073$ Å, $\mu(\text{Mo } K_\alpha) = 2.737$ mm⁻¹, $F(000) = 720$, $R = 0.0320$, $wR_2 = 0.0630$, $S = 1.011$, largest diff. Peak and hole: 0.279 and -0.343 e/Å³. CCDC-823410 contains the supplementary crystallographic data for this paper

Supplementary Material

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References and notes

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Fig. 1.
ORTEP diagram of **4g**

Fig. 2.
ORTEP diagram of **4u**

Scheme 1.
The synthesis of benzoazulen-1-one derivatives

Scheme 2.

Scheme 3.

Scheme 4.

Table 1Optimization of solvent and temperature for the synthesis of **4a** under MW

Entry	Solvent	T/°C	Time/min	Yield/%	
				4a	5
1	Benzene	90	16	10	61
2	DCE	90	16	15	57
3	THF	90	16	24	48
4	DMF	90	16	34	26
5	EtOH	90	16	45	21
6	Glycol	90	16	40	24
7	HOAc	90	14	55	trace
8	Water	90	16	51	trace

Table 2Regioselective synthesis of product **4a-n** under MW

Entry	4	R ₁	Time/min	Yield (%)
1	4a	4-Chlorophenyl (2a)	12	86
2	4b	4-Bromophenyl (2b)	12	85
3	4c	2,4-Dichlorophenyl (2c)	12	83
4	4d	4-Nitrophenyl (2d)	11	89
5	4e	4-Methylphenyl (2e)	15	83
6	4f	4-Methoxyphenyl (2f)	15	81
7	4g	2,3-Dimethoxyphenyl (2g)	15	78
8	4h	2-Thienyl (2h)	12	74
9	4i	Benzyl (2i)	16	70
10	4j	4-Chlorophenyl (2a)	10	87
11	4k	2,4-Dichlorophenyl (2b)	10	84
12	4l	4-Methylphenyl (2e)	13	81
13	4m	2-Thienyl (2h)	11	80
14	4n	Benzyl (2i)	15	76

Table 3

Synthesis of products **4o-4ll** under MW

Entry	4	R ₁	Time/min	Yield (%)
2	4p	4-Nitrophenyl (2d)	10	81
3	4q	4-Methylphenyl (2e)	9	83
4	4r	2-Thienyl (2h)	13	78
5	4s	Benzyl (2i)	12	80
6	4t	4-Chlorophenyl (2a)	15	75
7	4u	4-Bromophenyl (2b)	9	86
8	4v	2,4-Dichlorophenyl (2c)	9	86
9	4w	4-Nitrophenyl (2d)	8	88
10	4x	2-Chlorophenyl (2j)	7	85
11	4y	3-Nitrophenyl (2k)	9	84
12	4z	4-Cyanophenyl (2l)	7	87
13	4aa	Phenyl (2m)	8	89
14	4bb	4-Methylphenyl (2e)	11	83
15	4cc	2-Methoxyphenyl (2n)	12	82
16	4dd	3,4,5-Trimethoxyphenyl (2o)	12	79
17	4ee	4-Dimethylaminophenyl (2p)	15	76
18	4ff	2-Thienyl (2h)	14	73
19	4gg	Benzyl (2i)	11	79
20	4hh	Isobutyl (2q)	15	73
21	4ii	sec-butyl (2r)	16	72
22	4jj	1-Methylbutyl (2s)	17	72
23	4kk	Cyclohexyl (2t)	17	76
24	4ll	Isopropyl (2u)	16	75

Table 4Synthesis of products **5** under MW

Entry	Product	Time / min	Yield / %
1	5a , R ₄ = R ₂ = R ₃ = H	15	85
2	5b , R ₄ = OMe, R ₂ = R ₃ = H	18	83
3	5c , R ₄ = H, R ₂ = R ₃ = Me	20	88
4	5d , R ₄ = OMe, R ₂ = R ₃ = Me	24	86
5	5e , R ₄ = H, R ₂ = R ₃ = Cl	18	84
6	5f , R ₄ = OMe, R ₂ = R ₃ = Cl	18	82
7	5g , R ₄ = H, R ₂ = COOH, R ₃ = H	15	81
8	5h , R ₄ = OMe, R ₂ = COOH, R ₃ = H	16	80