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A NOVEL AND HIGHLY EFFICIENT PROTOCOL FOR THE SYNTHESIS OF CHALCONE BASED 1,2-DIAZEPINE AND 1,2-OXAZEPINE DERIVATIVES

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Abstract – A novel and highly efficient protocol is described for the synthesis of chalcone based 1,2-diazepine and 1,2-oxazepine derivatives. Under neat condition, the mixing and grinding of 1,5-diketones and hydrazine gave the cyclocondensation products in quantitative yields within 10-20 min at room temperature. Similarly, novel chalcone based 1,2-oxazepines were synthesized in excellent yields (85-88%) in 2-3 h at refluxed by the condensation of 1,5-diktones and hydroxylamine hydrochloride in water-ethanolic base.

INTRODUCTION

Substituted seven-membered heterocyclics like diazepine[1,2] and oxazepine[3,4] derivatives have received much attention in the recent years owing to their wide range of biological and pharmaceutical importance. An appropriate substitution and functionalization of diazepines and oxazepines have improved potentially their pharmacological properties. For example, some pyrrolo-based diazepines,[2c] oxazepines[3c] and their derivatives[3] have shown excellent biological activities (Figure 1).[5] Many other 1,2-oxazepine derivatives are known to be potential opioid analgesics[3b] and 1,2-diazepine derivatives are used as antihypertensive drugs and act as potential ACE inhibitors.[2b]

Due to the growing awareness about environmental concerns, organic chemists are under increasing pressure to alter current working practices for the greener and sustainable development in academia as well as industry research to find environmentally benign alternatives and efficient synthetic methods. Recently, there has been incredible interest in the synthetic manipulation of biologically active and functionalized indanedione derivatives.[6-8] Previous works have shown that fusing an indeno moiety to the core structure of a natural products enhanced the pharmacologic potential of a target molecule. Based on this veracity, the different derivatives have been synthesized as potential drug candidates in a wide range of bioactivities including antioxidants, anticoagulants, antibacterial, Cyclin-Dependent Kinases (CDK) inhibitors, neuroprotective agent,[9] and potential antitumor agents.[7]

We herein report a novel and highly efficient protocol in the synthesis of 1,2-diazepines and 1,2-oxazepines using chalcone and indeno moieties in search of pharmacologically active molecules. 1,2-Diazepines (4,5-dihydro indeno[1,2-*c*][1,2]diazepin-6(1*H*)-ones) synthesis is reported with 1,5-diketones and hydrazine in iso-propyl alcohol and acetic acid. This reaction has suffered with the use of acid catalyst, solvent, longer reaction time and high temperature.[10]

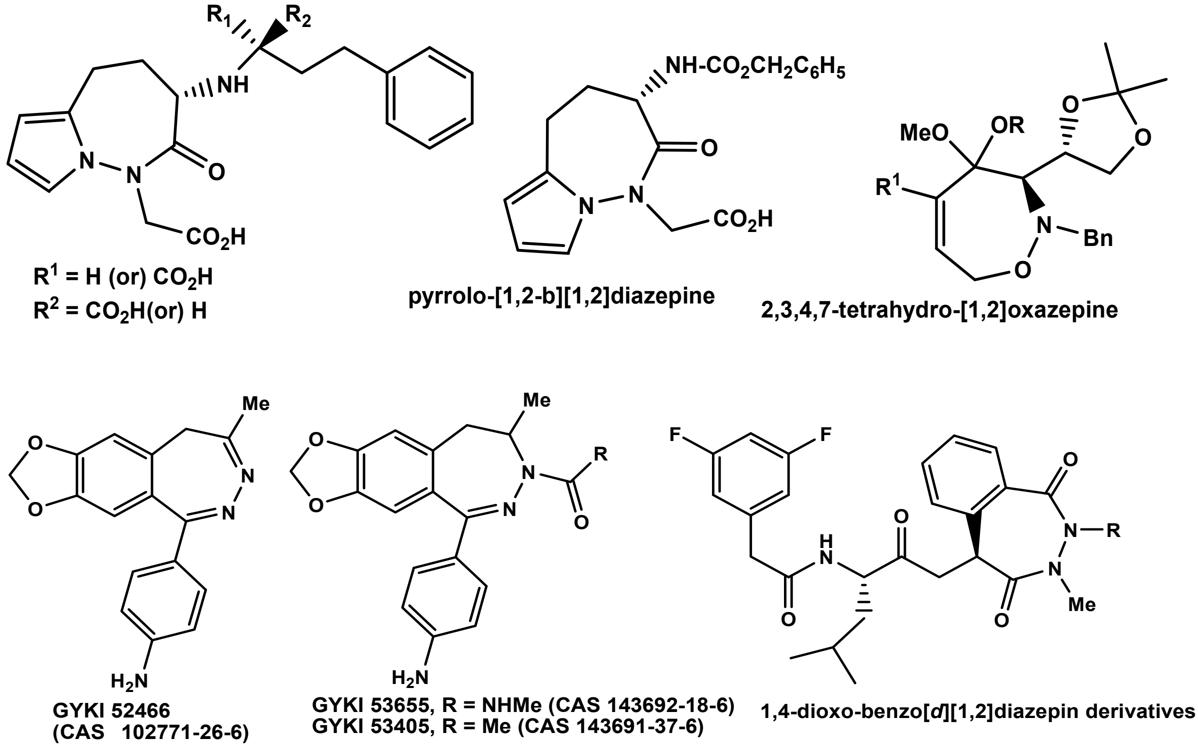


Figure 1. Bioactive diazepine and oxazepine molecules

RESULTS AND DISCUSSION

Reaction between 1,3-indanedione and chalcones

1,3-Indanedione[11] and chalcones[12] were prepared by following the literature procedures. Similarly, 1,5-diketones were obtained in excellent yields (80-95%) using 1,3-indanedione and chalcones with modification of reported method[13,14] in the presence of K_2CO_3 at 0 °C to room temperature in ethyl acetate. This method has advantage over previously reported procedures in yields and mild reaction conditions. We also tried other bases like NaOH, KOH, AcONa, NH_3, Et_3N, n-BuLi and Lewis acids like AcOH and ZnO, but they failed to give the products. The assigned structure of novel 1,5-diketones **3a-3u** was confirmed on the basis of their spectral analysis (IR, ^{1}H and ^{13}C-NMR, and ESI-MS) and others compared with available reported data in the literature.[13] For example, *2-[3-(4-chlorophenyl)-1-(3-nitrophenyl)-3-oxopropyl]-2H-indene-1,3-dione* **3b** found 92.0% pure in hplc analysis, the IR spectral peaks at 1730, 1703 cm^{-1} showed the presence of saturated carbonyl groups. The ^{1}H NMR spectrum contained peak at δ 3.37 ppm (d, *J* = 8.0 Hz, 1H), in which the coupling constant (*J* = 8.0 Hz) indicated the indandione ring proton at 2-position coupled with a trans proton. Peak at δ 4.41 ppm (m, 1H) indicated for Ar-$C\underline{H}$-CH$_2$-proton, coupled with three adjacent protons. Similarly, peaks at δ 4.17 ppm (dd, *J* = 13.0 Hz, 7.0 Hz, 1H) and 3.52 ppm (dd, *J* = 13.0 Hz, 7.0 Hz, 1H) indicated the diastereotopic protons of Ar-CH-C$\underline{H}_a$-(CO)-Ar and Ar-(CH)-C$\underline{H}_b$-(CO)-Ar, respectively. The ^{13}C NMR spectrum gave peaks at δ 199.5, 198.5 and 196.5 ppm for three characteristic carbonyl carbons, 56.71 ppm for indandione carbon, 40.66 ppm for Ar-$\underline{C}H$-CH$_2$-carbon and 38.8 ppm for Ar-CH-$\underline{C}H_2$-CO-Ar carbon. ESI-MS also gave the molecular ion peak at 434 [M+H$^+$] for compound **3b**. Similarly, other derivatives **3a, 3c-3u** were confirmed on their spectral analysis (experimental section).

Reaction between 1,5-diketone and hydrazine

Initially, the reaction was carried out between 1,5-diketones and hydrazine in 1:1 and 1:2 molar ratios respectively under neat condition. However, 1,5-diketones remained unconsumed and poor yields was obtained even prolonging the reaction time at room temperature (Table 1, entries 1 & 2). Then, we carried out the reaction using 1,5-diketone and hydrazine in 1:3 molar ratio in the presence of p-toluenesulfonic acid (PTSA) catalyst in EtOH at room temperature. The product was obtained in good yields (75%) in 2.30 h (Table 1, entry 3). The reaction was serendipitously improved in yields (96%) by grinding under neat condition for 10-20 min in the later molar ratio (Table 1, entry 4). The purity of the product was good enough for spectral analysis. Based on the optimized molar ratio (1:3) under grinding and neat condition, all products **4a-r** was obtained in excellent yields (Table 2). In the case of 2'-aminochalcone based 1,5-diketones **3s-3u**, the reaction with hydrazine in the optimized reaction condition gave the low yields even prolonged reaction time (Table 2). This might be due to the stronger hydrogen bonding between carbonyl oxygen and NH$_2$ group, which stalled the water elimination and so the reaction became sluggish. However, we got the products in moderate yields (30-40%) in heating condition at 80-85 °C. In the case of 2'-hydroxychalcone based 1,5-diketones **3o-3r**, the reaction with hydrazine in the optimized reaction condition gave good yield within 10-20 min (Table 2). This might be due to the poor hydrogen bonding between carbonyl oxygen and OH group compared to amino group.

Table 1. Optimization of cyclocondensation reaction in **3b**

s.no	1,5-diketone:N_2H_4(mmol)	rxn. time (min)	yield (%)
1	1:1	20 - 50[a]	35
2	1:2	20 - 50[a]	60
3	1:3	120 -150[b]	75
4	**1:3**	**10 - 20**[a]	**96**

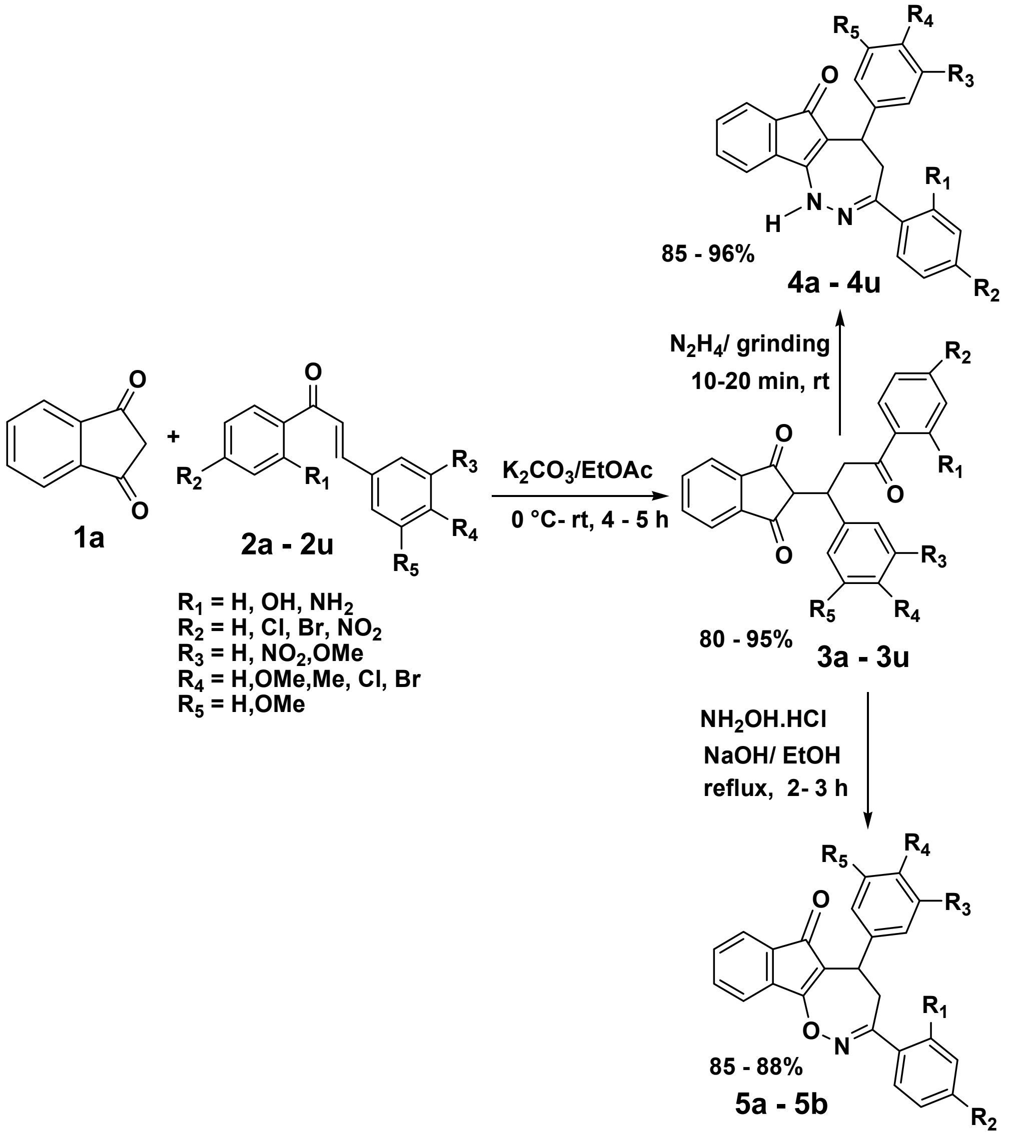
[a] reaction in neat grinding. [b] reaction with PTSA stirred in EtOH at rt.

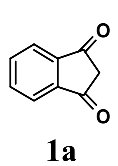
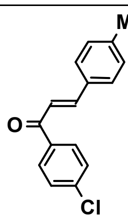
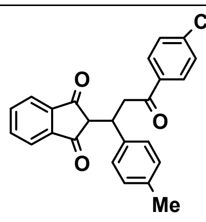
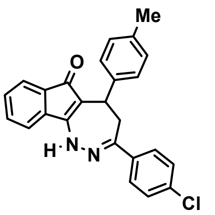
All new products were confirmed by their spectral analysis (IR, ^{1}H- and ^{13}C-NMR, and ESI-MS) and others compared with reported data in the literature.[10] For example, *(2E,5aE)-3-(4-chlorophenyl)-5-(3-nitrophenyl)-4,5-dihydroindeno[1,2-c][1,2]diazepin-6(1H)-one* **4b**, the IR spectral peaks at 3434, 1681 cm^{-1} observed due to NH and carbonyl groups respectively. The ^{1}H NMR spectrum contained peak at δ 4.70 ppm (dd, *J* = 5.0 Hz, 2.0 Hz, 1H), in which the coupling constant (*J* = 5.0 Hz) indicated for Ar-$C\underline{H}$-CH_2-cyclic proton of diazepine ring. Peaks at δ 3.42 ppm (dd, *J* = 13.5 Hz, 5.0 Hz, 1H) and 3.07 ppm (dd, *J* = 13.5 Hz, 3.0 Hz, 1H) indicated for Ar-CH-$C\underline{H}_a$- and Ar-CH-$C\underline{H}_b$-diazepine ring diastereotopic protons. The ^{13}C NMR spectrum gave peaks at δ 191.15 ppm for the characteristic carbonyl carbon, 40.51 ppm for Ar-$\underline{C}H$-CH_2, and 38.11 ppm for Ar-CH-$\underline{C}H_2$- of diazepine ring carbons. Further, ESI-MS showed the molecular ion peak at 430.0962 [M+H$^+$] for the compound **4b**. Similarly, other derivatives **4a, 4c-4r** were confirmed on their spectral analysis (experimental section).

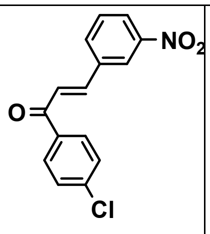
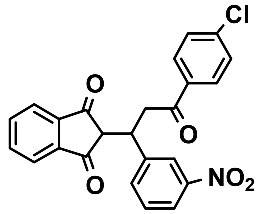
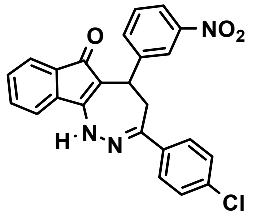
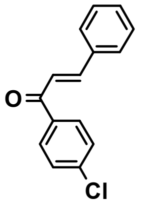
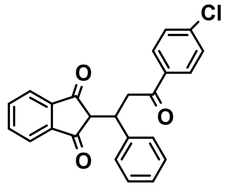
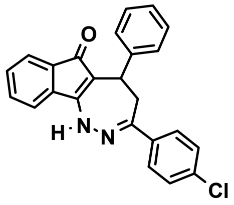
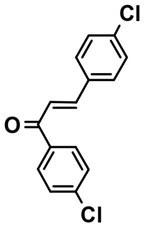
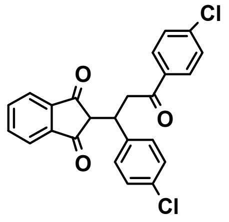
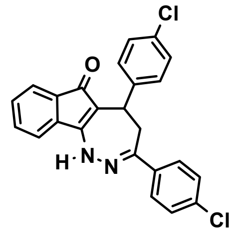
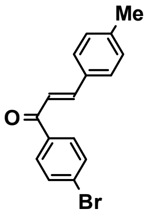
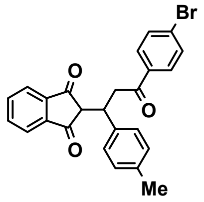
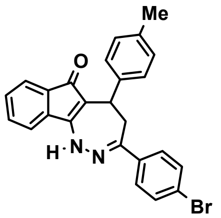
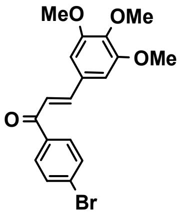
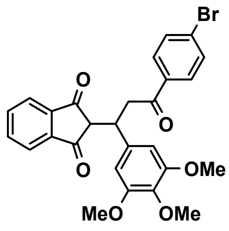
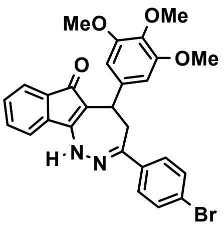
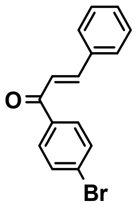
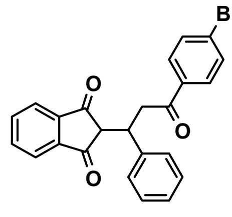
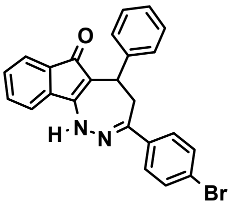
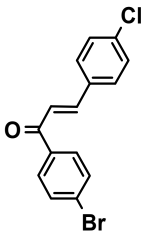
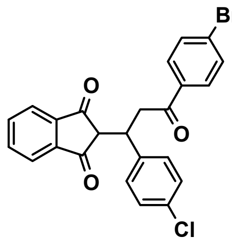
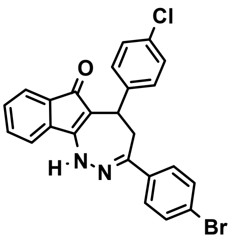
Reaction between 1,5-diketone and $NH_2OH{\cdot}HCl$

The reaction between 1,5-diketones and $NH_2OH.HCl$ in 1:1, 1:2 and 1:3 molar ratios gave poor or no yield in the presence of base under grinding and/or neat condition even prolonging the reaction time at room temperature or heating conditions. Then, we carried out this reaction in 1:2 molar ratio in water ethanolic base at refluxed temperature, which gave 1,2-oxazepines in excellent yields (85-88%) within 2-3 h. These products were confirmed by their spectral analysis like IR, ^{1}H- and ^{13}C-NMR and ESI-MS. For example, *(2E,5aE)-3-(4-bromophenyl)-5-phenyl-4,5-dihydroindeno[2,1-f][1,2]oxazepin-6-one* **5b**, the IR spectral peak at 1685 cm^{-1} indicated a carbonyl group. The ^{1}H NMR spectrum peak at δ 5.68 ppm (dd, *J* = 8.5 Hz, 2.5 Hz, 1H) showed Ar-$C\underline{H}$-CH_2- proton of oxazepine ring, in which the coupling constant (*J* = 8.0 Hz and 2.5 Hz) indicated the presence of *trans* and *cis* protons. Peaks at δ 3.66 ppm (dd, *J* = 12.5 Hz, 8.5 Hz, 1H) and 3.24 ppm (dd, *J* = 13.0 Hz, 8.0 Hz, 1H) indicated geminal and trans coupling of Ar-CH-$C\underline{H}_a$- with Ar-CH-$C\underline{H}_b$- and Ar-$C\underline{H}$-$C\underline{H}_2$-oxazepine ring diastereotopic protons respectively. The ^{13}C NMR spectrum gave peak at δ 193.10 ppm for the characteristic carbonyl carbon, 42.85 ppm for Ar-*C̲H*-CH$_2$, and 39.64 ppm for Ar-CH-*C̲H$_2$* of oxazepine ring carbons. Further, ESI-MS showed the molecular ion peak at 430.0440 [M+H$^+$] for the compound **5b**. Similarly, **5a** was confirmed on their spectral analysis (experimental section).

Table 2. Synthesis of 1,5-diketone, 1,2-diazepine and 1,2-oxazepine derivatives



Indanedione	Chalcone	1,5-Diketone	Yield (%)	Diazepin/Oxazepin	Yield (%)
 1a	 2a	 3a	90	 4a	93[a]

1a	 **2b**	 **3b**	92	 **4b**	95[a]
1a	 **2c**	 **3c**	91	 **4c**	95[a]
1a	 **2d**	 **3d**	89	 **4d**	94[a]
1a	 **2e**	 **3e**	95	 **4e**	91[a]
1a	 **2f**	 **3f**	87	 **4f**	90[a]
1a	 **2g**	 **3g**	92	 **4g**	93[a]
1a			92		96[a]

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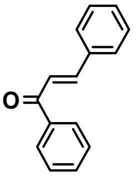
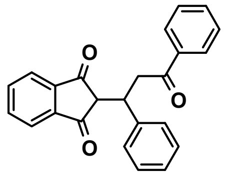
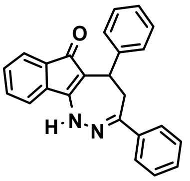
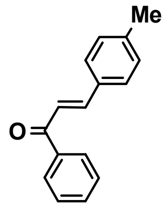
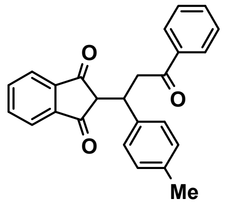
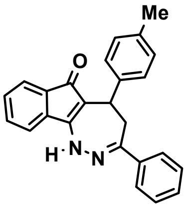
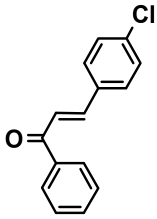
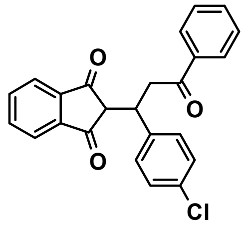
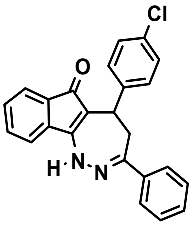
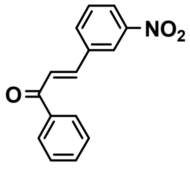
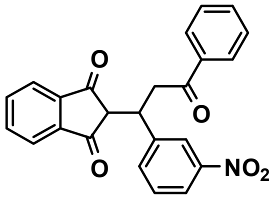
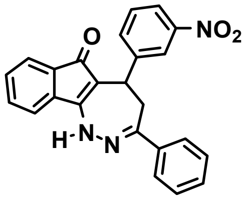
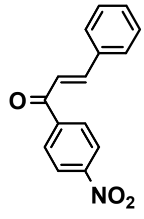
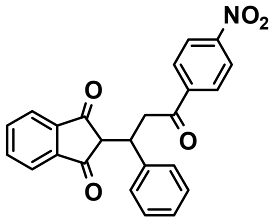
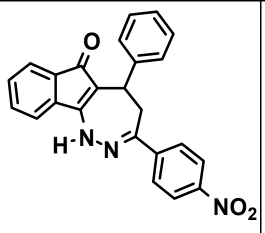
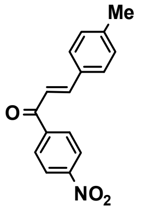
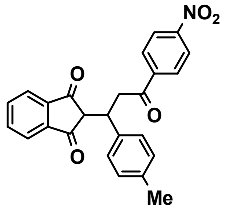
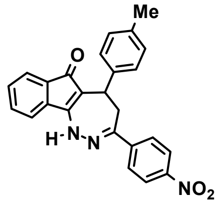
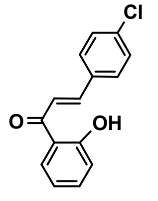
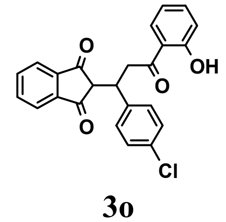
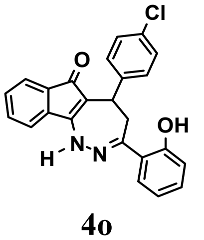
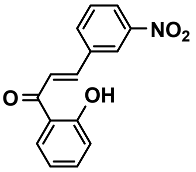
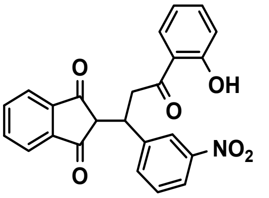
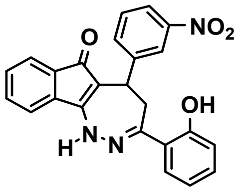
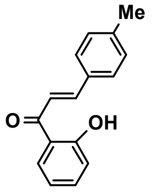
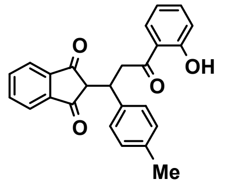
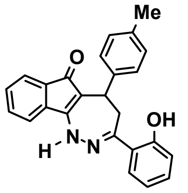
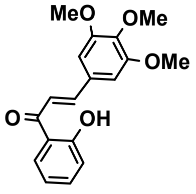
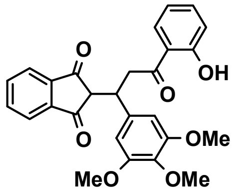
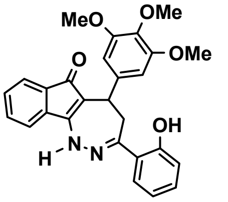
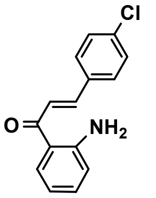
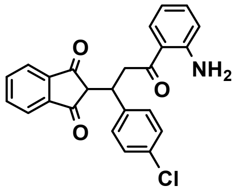
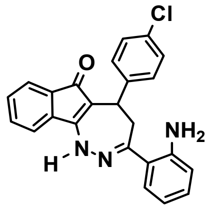
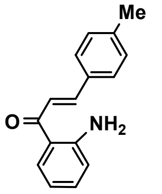
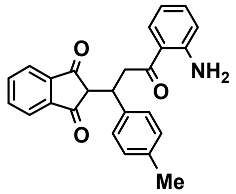
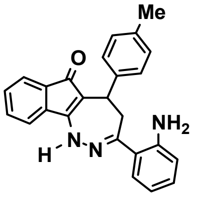
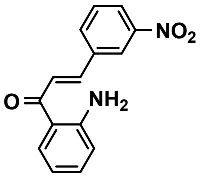
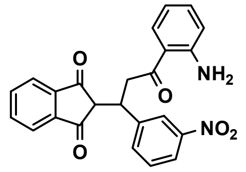
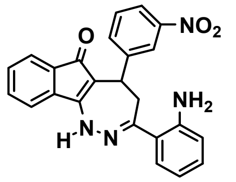
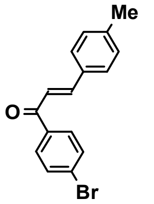
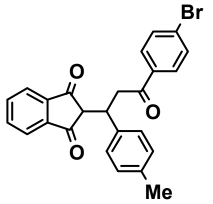
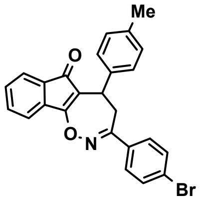
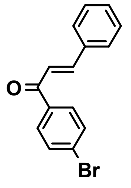
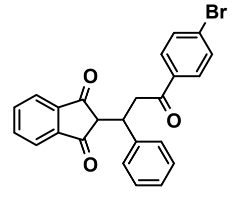
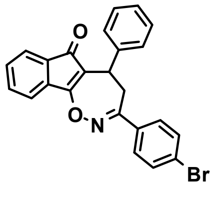
1a	 **2i**	 **3i**	94	 **4i**	96[a]
1a	 **2j**	 **3j**	93	 **4j**	94[a]
1a	 **2k**	 **3k**	90	 **4k**	95[a]
1a	 **2l**	 **3l**	91	 **4l**	91[a]
1a	 **2m**	 **3m**	89	 **4m**	92[a]
1a	 **2n**	 **3n**	88	 **4n**	92[a]
1a	 **2o**	 **3o**	87	 **4o**	89[a]

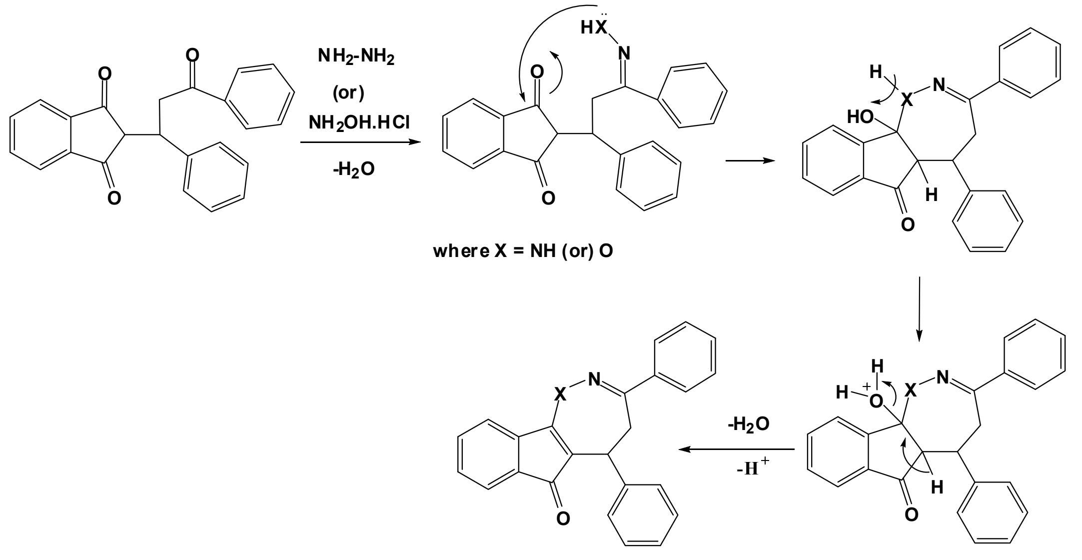
1a	 **2p**	 **3p**	89	 **4p**	85^{a}
1a	 **2q**	 **3q**	88	 **4q**	87^{a}
1a	 **2r**	 **3r**	89	 **4r**	90^{a}
1a	 **2s**	 **3s**	85	 **4s**	40^{b}
1a	 **2t**	 **3t**	83	 **4t**	36^{b}
1a	 **2u**	 **3u**	80	 **4u**	30^{b}
1a	 **2e**	 **3e**	95	 **5a**	85^{c}

1a	 **2g**	 **3g**	92	 **5b**	88[c]

[a] reaction time 10-20 min neat grinding. [b] reaction time 10-20 min at 80 °C. [c] reaction time 2-3 h reflux.

In conclusion, we have reported a novel, highly efficient protocol for the synthesis of chalcone based 1,2-diazepines and 1,2-oxazepines. Under neat condition, grinding of 1,5-diketones and hydrazine gave the cyclocondensation products (1,2-diazepines) in quantitative yields within 10-20 min at room temperature. Similarly, novel chalcone based 1,2-oxazepines were obtained by the condensation of 1,5-diktones and hydroxylamine hydrochloride in excellent yields (85-88%) at refluxed in 2-3 h using water-ethanolic base.

MECHANISM



EXPERIMENTAL

General Methods: Organic solvents were dried by standard methods when necessary. Commercially available reagents were used without further purification unless mentioned. All reactions were monitored by TLC using precoated silica gel aluminum plates. Visualization of TLC plates was accomplished with UV lamp or in iodine chamber. The column chromatography was performed using silica gel 100–200 mesh size (SD Fine-Chem Limited) with ethyl acetate/hexanes as an eluent system. Melting points were recorded on perfit apparatus and are uncorrected. IR spectra of the compounds were expressed as wave numbers (cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively. ^{1}H NMR spectra were recorded in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. Chemical shifts of ^{1}H NMR spectra were given in parts per million with respect to TMS, and the coupling constant J was measured in Hz. Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet). Mass spectra were recorded by EI-MS and HRMS. Purity of compounds **3a-3u** was determined by HPLC (SHIMADZU LC-2010AHT, UV detector (λ_{max} 260 nm) using LICHROSPHER-100 (RP-C18) column.

General Procedure: (a) *Synthesis of 1,5-diketones*: A mixture of indanedione (1.1 mmol) and K_2CO_3 (1.2 mmol) was dissolved in EtOAc (4 mL) and cooled to 0 °C. Chalcone (1.0 mmol) dissolved in EtOAc (3 mL) was added dropwise in the above stirred mixture at 0 °C. Followed by, the reaction mixture was slowly warmed at room temperature. TLC monitoring, the reaction mixture was poured into water (4-5 h) and extracted with EtOAc (3 x 10 mL). The combined organic layer was dried over anhy. $MgSO_4$ and the solvent was evaporated under vacuum. The residue was recrystalized with suitable solvent (MeOH) to afford excellent yields (upto 95%) as a solid.

2-(3-(4-Chlorophenyl)-3-oxo-1-*p*-tolylpropyl)-2*H*-indene-1,3-dione (3a): Yellow solid. Yield: 362.6 mg (90%). Mp 118-120 °C. IR ν_{max} (KBr, cm^{-1}): 3132, 3017 (aromatic C-H str), 1720, 1703 (C=O str), 1588 (aromatic, C=C str), 1400, 1254, 1198, 1087, 817, 766. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.26 (m, 1H), 4.17 (dd, J = 10.0 Hz, 4.0 Hz, 1H), 3.54 (m, 2H), 2.17 (s, 3H), 7.94 (d, J = 9.0 Hz, 2H), 7.86 (d, J = 7.0 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.72 (m, 2H) 7.43 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.0, 198.7, 196.8 (C=O), 141.9, 141.6, 139.0, 136.6, 136.0, 134.7, 134.7, 134.5, 128.9, 128.5, 128.2, 127.9, 127.5, 122.3, 122.1, 56.1, 40.3, 38.4, 20.2. MS (ESI): m/z (%) 403 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{25}H_{19}ClO_3$: 403.1101; found 403.1092. HPLC-purity 94.5%.

2-(3-(4-Chlorophenyl)-1-(3-nitrophenyl)-3-oxopropyl)-2*H*-indene-1,3-dione (3b): Yellow solid. Yield: 398 mg (92%). Mp 123-125 °C. IR ν_{max} (KBr, cm^{-1}): 3153, 2918, 1730, 1703 (C=O str), 1524 (aromatic, C=C str), 1402, 1348, 1268, 1210, 1093, 828. ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm): 4.41 (m, 1H), 4.17(dd, J = 13.0 Hz, 7.0 Hz, 1H), 3.52 (dd, J = 12.5 Hz, 7.5 Hz, 1H), 3.37 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 6.5 Hz, 1H), 8.07 (m, 1H), 7.90 (m, 2H), 7.84 (m, 2H), 7.79 (m, 1H), 7.73 (m, 1H), 7.68 (m, 1H), 7.54 (m, 2H), 7.43 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 199.5, 198.5, 196.5 (C=O), 148.2, 142.7, 142.3, 142.0, 140.1, 135.9, 135.1, 134.8, 129.6, 129.5, 129.2, 129.1, 123.2, 123.2, 122.4, 56.7, 40.7, 38.8. MS (ESI): m/z (%): 434 [M+H$^+$] $C_{24}H_{16}ClNO_5$. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{16}ClNO_5$: 434.0795; found 434.0780. HPLC-purity 92.0%.

2-(3-(4-Chlorophenyl)-3-oxo-1-phenylpropyl)-2*H*-indene-1,3-dione (3c): Yellow solid. Yield: 354 mg (91%). Mp 124-126 °C. IR ν_{max} (KBr, cm^{-1}): 3049, 2945, 1718, 1699 (C=O str), 1518 (aromatic, C=C str), 1430, 1355, 1249, 1225, 1075, 810. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.31 (m, 1H), 4.13 (m, 1H), 3.61 (dd, *J* = 18.0 Hz, 5.0 Hz, 1H), 3.52 (d, *J* = 8.5 Hz, 1H) 7.92 (m, 2H), 7.80 (m, 2H), 7.72 (m, 2H), 7.63 (m, 1H), 7.43 (m, 2H), 7.19 (m, 2H), 7.12 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.3, 199.1, 198.2 (C=O), 142.5, 138.9, 136.7, 135.6, 135.5, 133.3, 132.8, 129.8, 129.6, 129.2, 128.7, 128.6, 128.1, 123.1, 122.0, 56.8, 40.8, 38.8. MS (ESI): m/z (%) 389 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}ClO_3$: 389.0944; found 389.0928. HPLC-purity 91.8%.

2-(1,3-Bis(4-chlorophenyl)-3-oxopropyl)-2*H*-indene-1,3-dione (3d): Yellow solid. Yield: 376.5 mg (89%). Mp 123-125 °C. IR ν_{max} (KBr, cm^{-1}): 3085, 3013 (aromatic C-H str), 1711, 1679 (C=O str), 1575 (aromatic, C=C str), 1421, 1345, 1211, 1087, 1005, 810, 765. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.29 (m, 1H), 4.12 (m, 1H), 3.72 (m, 1H), 3.58 (m, 1H), 7.83 (m, 2H), 7.74 (m, 2H), 7.40-7.38 (m, 4H), 7.18 (dd, *J* = 7.0 Hz, 1.5 Hz, 2H) 7.10 (dd, *J* = 7.0 Hz, 1.5 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.4, 199.0, 197.0 (C=O), 143.8, 142.5, 139.9, 138.8, 136.7, 136.3, 135.7, 135.1, 133.0, 129.9, 129.7, 128.7, 128.4, 123.1, 123.0, 121.9, 56.7, 40.8, 38.8. MS (ESI) m/z (%) 423 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{16}Cl_2O_3$: 423.0555; found 423.0548. HPLC-purity 94.2%.

2-(3-(4-Bromophenyl)-3-oxo-1-p-tolylpropyl)-2*H*-indene-1,3-dione (3e): Yellow solid. Yield: 424.6 mg (95%). Mp 120-122 °C. IR ν_{max} (KBr, cm^{-1}): 3135, 2914 (aromatic C-H str), 1739, 1705 (C=O str), 1672, 1590 (aromatic, C=C str), 1400, 1255, 1200, 1072, 813. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.26 (m, 1H), 4.15(dd, *J* = 11.0 Hz, 5.0 Hz, 1H), 3.52 (m, 2H), 2.17 (s, 3H), 7.81 (m, 3H), 7.79 (m, 1H), 7.72 (m, 2H), 7.60 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 7.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.7, 199.4, 197.7 (C=O), 145.6, 142.6, 142.3, 137.3, 136.7, 135.7, 135.4, 131.9, 130.0, 129.8, 129.2, 128.6, 128.2, 123.0, 122.9, 120.5, 56.9, 41.7, 39.2, 20.9. MS (ESI): m/z (%) 447 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{19}BrO_3$: 447.0596; found 447.0580. HPLC-purity 94.0%.

2-(3-(4-Bromophenyl)-3-oxo-1-(3,4,5-trimethoxy phenyl)propyl)-2*H*-indene-1,3-dione (3f): Yellow solid. Yield: 455 mg (87%). Mp 132-134 °C. IR ν_{max} (KBr, cm^{-1}): 3104, 2930 (aromatic C-H str), 1725, 1701 (C=O str), 1587 (aromatic, C=C str), 1505, 1456, 1405, 1253, 1122, 1090, 821,763. ^{1}H-NMR ($CDCl_3$, 500MHz) δ (ppm): 4.22 (m, 1H), 4.10 (m, 1H), 3.54 (m, 2H), 3.74 (s, 6H), 3.69 (s, 3H), 7.84 (m, 4H), 7.75 (m, 2H), 7.61 (d, *J* = 8.5 Hz, 2H), 6.44 (s, 2H). ^{13}C-NMR ($CDCl_3$, 125MHz) δ (ppm): 200.8, 199.4, 197.5 (C=O), 152.9, 142.7, 142.4, 136.8, 136.1, 135.6, 135.5, 132.0, 129.7, 129.1, 128.9, 128.5, 123.1, 122.1, 105.4, 60.7, 56.9, 56.1, 41.0, 40.2. MS (ESI): m/z (%) 523 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{27}H_{23}BrO_6$: 523.0756; found 523.0750. HPLC-purity 93.7%.

2-(3-(4-Bromophenyl)-3-oxo-1-phenylpropyl)-2*H*-indene-1,3-dione (3g): Yellow solid. Yield: 398 mg (92%). Mp 121-123 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3110, 3015, 2987 (aromatic C-H str), 1731, 1701 (C=O str), 1545 (aromatic, C=C str), 1468, 1387, 1221, 1097, 1045, 812. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.29 (m, 1H), 4.15 (m, 1H), 3.54 (m, 2H), 7.89 (dd, *J* = 6.0 Hz, 1.5 Hz, 2H), 7. 71 (m, 2H), 7.68 (m, 2H), 7.58 (m, 2H), 7.21 (m, 2H), 7.07 (m, 3H). ^{13}C-NMR ($CDCl_3$, 125MHz) δ (ppm): 200.6, 199.3, 197.6 (C=O), 142.6, 142.3, 140.3, 135.6, 135.4, 131.9, 129.9, 129.4, 128.7, 128.5, 127.4, 127.2, 126.9, 123.0, 122.9, 56.8, 40.9, 39.6. MS (ESI): m/z (%) 433 [M+H^{+}]. HRMS-ESI (m/z): [M+H^{+}] calcd for $C_{24}H_{17}BrO_3$: 433.0439; found 433.0422. HPLC-purity 92.3%.

2-(3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl)-2*H*-indene-1,3-dione (3h): Yellow solid. Yield: 429 mg (92%). Mp 120-122 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3045, 2987 (aromatic C-H str), 1710, 1697 (C=O str), 1545 (aromatic, C=C str), 1420, 1329, 1189, 1121, 1023, 791. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.17 (m, 1H), 4.02 (dd, *J* = 18.0 Hz, 3.0 Hz, 1H), 3.49 (dd, *J* = 17.0 Hz, 4.0 Hz, 1H), 3.43 (d, *J* = 7.5 Hz, 1H), 7.84 (m, 2H), 7.77 (d, *J* = 6.5 Hz, 1H), 7.71 (d, *J* = 7.0 Hz, 1H), 7.62 (m, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.37 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz 1H), 7.03 (d, *J* = 8.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.3, 200.0, 197.0 (C=O), 143.9, 142.4, 142.2, 139.8, 139.4, 135.7, 135.0, 132.3, 131.3, 130.2, 129.9, 129.5, 129.0, 123.1, 123.0, 121.1, 56.7, 40.7, 38.8. MS (ESI): m/z (%) 467 [M+H^{+}]. HRMS-ESI (m/z): [M+H^{+}] calcd for $C_{24}H_{16}BrClO_3$: 467.0050; found 467.0032. HPLC-purity 96.0%.

2-(3-Oxo-1,3-diphenylpropyl)-2*H*-indene-1,3-dione (3i): Yellow solid. Yield: 333.6 mg (94%). Mp 129-131 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3118, 3010, 2935 (aromatic C-H str), 1742, 1703 (C=O str), 1572, 1513 (aromatic, C=C str), 1425, 1379, 1156, 1035, 756. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.18 (m, 1H), 4.06 (m, 1H) 3.43 (m, 2H), 7.56 (m, 2H), 7.48 (m, 2H), 7.38 (m, 2H), 7.33 (m, 2H), 7.29 (m, 1H), 7.18 (m, 1H), 7.15 (m, 2H), 6.96 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.6, 199.4, 198.5, (C=O), 144.8, 142.6, 140.6, 138.2, 136.9, 135.2, 133.1, 132.9, 131.0, 130.6, 129.3, 128.7, 128.5, 122.9, 122.0, 56.9, 40.9, 39.6. MS (ESI): m/z (%) 355 [M+H^{+}]. HRMS-ESI (m/z): [M+H^{+}] calcd for $C_{24}H_{18}O_3$: 355.1334; found 355.1320. HPLC-purity 91.8%.

2-(3-Oxo-3-phenyl-1-p-tolylpropyl)-2*H*-indene-1,3-dione (3j): Yellow solid. Yield: 343.17 mg (93%). Mp 125-127 °C. IR ν_{max} (KBr, cm^{-1}): 3102, 2997 (aromatic C-H str), 1735, 1699 (C=O str), 1536 (aromatic, C=C str), 1478, 1389, 1252, 1121, 1066, 813. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.16 (m, 1H), 4.07 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.45 (m, 2H), 2.03 (s, 3H), 7.86 (d, *J* = 7.0 Hz, 2H), 7.70 (d, *J* = 7.0 Hz, 1H), 7.64 (d, *J* = 7.0 Hz, 1H), 7.50 (m, 2H), 7.40 (m, 2H), 7.10 (m, 3H), 6.80 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.7, 199.5, 198.7 (C=O), 144.9, 142.6, 142.3, 141.1, 138.3, 137.5, 136.9, 135.4, 133.2, 132.7, 131.0, 129.8, 129.1, 129.0, 123.0, 121.1, 57.0, 41.1, 39.3, 20.7. MS (ESI): m/z (%) 369 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{25}H_{20}O_3$: 369.1491; found 369.1495. HPLC-purity 93.0%.

2-(1-(4-Chlorophenyl)-3-oxo-3-phenylpropyl)-2*H*-indene-1,3-dione (3k): Yellow solid. Yield: 350 mg (90%). Mp 126-128 °C. IR ν_{max} (KBr, cm^{-1}): 3053, 2948, 1722, 1698 (C=O str), 1514 (aromatic, C=C str), 1432, 1352, 1251, 1221, 1073, 808. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.30 (m, 1H), 4.15 (m, 1H), 3.63 (dd, J = 13.0 Hz, 5.0 Hz, 1H), 3.54 (d, J = 6.0 Hz, 1H), 7.90 (m, 2H), 7.84 (m, 2H), 7.75 (m, 2H), 7.61 (m, 1H), 7.46 (m, 2H), 7.20 (m, 2H), 7.10 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.4, 199.1, 198.2 (C=O), 142.5, 139.0,136.8, 135.6, 135.6, 133.4, 132.9, 129.9, 129.6, 129.3, 128.7, 128.6, 128.1, 123.1, 122.0, 56.9, 40.8, 38.8. MS (ESI): m/z (%) 389 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}ClO_3$: 389.0944; found 389.0950. HPLC-purity 92.4%.

2-(1-(3-Nitrophenyl)-3-oxo-3-phenylpropyl)-2*H*-indene-1,3-dione (3l): Yellow solid. Yield: 363 mg (91%). Mp 134-136 °C. IR ν_{max} (KBr, cm^{-1}): 3095, 3043 (aromatic C-H str), 1705, 1675 (C=O str), 1587 (aromatic, C=C str), 1485, 1399, 1235, 1177, 1090, 817 (C-Cl, str). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.37 (m, 1H), 4.05 (m, 1H) 3.64 (dd, J = 13.5 Hz, 6.0 Hz, 1H), 3.50 (m, 1H), 8.10 (d, J = 7.0 Hz, 1H), 7.90-7.85 (m, 3H), 7.76 (d, J = 7.5 Hz, 1H), 7.68 (m, 2H), 7.58 (d, J = 7.5 Hz, 1H), 7.49 (t, J = 7.0 Hz, 1H), 7.38 (m, 2H), 7.20 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 199.5, 198.6, 197.7 (C=O), 148.2, 142.9, 142.3, 142.0, 136.5, 135.8, 135.1, 133.6, 129.5, 128.8, 128.6, 128.3, 128.1, 124.7, 123.3, 123.2, 122.3, 56.8, 40.7, 38.9. MS (ESI): m/z (%) 400 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}NO_5$: 400.1185; found 400.1173. HPLC-purity 93.2%.

2-(3-(4-Nitrophenyl)-3-oxo-1-phenylpropyl)-2*H*-indene-1,3-dione (3m): Yellow solid. Yield: 355 mg (89%). Mp 120-122 °C. IR ν_{max} (KBr, cm^{-1}): 3067, 2982 (aromatic C-H str), 1735, 1710 (C=O str), 1563 (aromatic, C=C str), 1425, 1352, 1232, 1141, 1096, 824. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.20 (m, 2H), 3.55 (dd, J = 11.0 Hz, 3.0 Hz, 1H), 3.45 (d, J = 6.0 Hz, 1H), 8.17 (d, J = 8.0 Hz, 2H), 8.01 (m, 2H), 7.76 (d, J = 7.5 Hz, 1H), 7.68 (d, J = 7.0 Hz, 1H), 7.61 (m, 2H), 7.18 (m, 2H), 7.11 (m, 2H), 6.95 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.6, 199.2, 197.2 (C=O), 150.4, 142.5, 142.3, 141.3, 139.9, 135.6, 135.6, 129.2, 128.6, 128.3, 127.3, 123.9, 123.0, 122.9, 56.6, 41.6, 39.5.MS (ESI): m/z (%) 400 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}NO_5$: 400.1185; found 400.1171. HPLC-purity 92.0%.

2-(3-(4-Nitrophenyl)-3-oxo-1-*p*-tolylpropyl)-2*H*-indene-1,3-dione (3n): Yellow solid. Yield: 363 mg (88%). Mp 127-129 °C. IR ν_{max} (KBr, cm^{-1}): 3075, 2998 (aromatic C-H str), 1710, 1698 (C=O str), 1557 (aromatic, C=C str), 1458, 1359, 1204, 1154, 1040, 799. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.27 (m, 2H), 3.62 (m, 1H), 3.53 (m, 1H), 2.13 (s, 3H), 8.28 (m, 2H), 8.13 (m, 2H), 7.85 (d, J = 7.0 Hz, 1H), 7.79 (d, J = 6.0 Hz, 1H), 7.71 (m, 2H), 7.22 (d, J = 7.5 Hz, 2H), 6.91 (d, J = 8.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.7, 199.2, 197.3 (C=O), 150.3, 142.6, 142.3, 141.3, 136.9, 135.5, 131.6, 129.9, 129.4, 128.8, 123.9, 123.0, 122.9, 120.3, 56.6, 40.7, 39.1, 20.9. MS (ESI): m/z (%) 414 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{25}H_{19}NO_5$: 414.1341; found 414.1349. HPLC-purity 90.1%.

2-(1-(4-Chlorophenyl)-3-(2-hydroxyphenyl)-3-oxopropyl)-2*H*-indene-1,3-dione (3o): Yellow solid. Yield: 351.5 mg (87%). Mp 116-118 °C. IR ν_{max} (KBr, cm^{-1}): 3434 (-OH str), 3110, 2912 (aromatic C-H str), 1722, 1710 (C=O str), 1638 (aromatic, C=C str), 1480, 1443, 1253, 1154, 981, 853, 758. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.28 (m, 1H), 4.20 (dd, J = 17.5 Hz, 9.5 Hz, 1H), 3.76 (dd, J = 17.5 Hz, 5.0 Hz, 1H), 3.50 (d, J = 7.0 Hz, 1H), 12.07 (s, br, D_2O exchangeble, 1H), 7.92 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.86 (dd, J = 6.0 Hz, 1.5 Hz, 1H), 7.81 (m, 1H), 7.71 (m, 1H), 7.57 (m, 1H), 7.47 (m, 1H), 7.11 (d, J = 7.5 Hz, 2H), 6.93 (m, 4H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 201.0, 200.1, 198.9 (C=O), 162.4, 142.4, 142.1, 138.4, 136.6, 135.7, 135.6, 133.0, 129.9, 129.7, 128.6, 123.1, 122.9, 119.3, 119.1, 118.5, 56.8, 40.2, 38.5. MS (ESI): m/z (%) 405 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}ClO_4$: 405.0984; found 405.0970. HPLC-purity 91.0%.

2-(3-(2-Hydroxyphenyl)-1-(3-nitrophenyl)-3-oxopropyl)-2*H*-indene-1,3-dione (3p): Yellow solid. Yield: 369.2 mg (89%). Mp 182-184 °C. IR ν_{max} (KBr, cm^{-1}): 3420 (-OH str), 3115, 2952 (aromatic C-H str), 1723, 1715 (C=O str), 1638 (aromatic, C=C str), 1485, 1405, 1248, 1179, 990, 820, 760. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.45 (m, 1H), 4.17 (dd, J = 18.0 Hz, 8.5 Hz, 1H), 3.76 (dd, J = 18.0 Hz, 6.5 Hz, 1H), 3.55 (d, J = 4.0 Hz, 1H), 11.89 (s, br, D_2O exchangeble, 1H), 8.17 (d, J = 1.5 Hz, 1H), 7.98 (dd, J = 8.5 Hz, 1.5 Hz, 1H), 7.90 (dd, J = 6.0 Hz, 2.0 Hz, 2H), 7.86 (m, 1H), 7.76 (m, 2H) 7.65 (d, J = 12.0 Hz, 1H), 7.47 (m, 1H), 7.36 (t, J = 8.0 Hz, 1H), 6.95 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 203.3, 199.3, 198.4 (C=O), 162.3, 148.1, 142.3, 142.2, 141.9, 136.8, 135.9, 134.9, 129.8, 129.5, 123.2, 122.4, 119.2, 118.6, 56.7, 40.1, 38.5. MS (ESI): m/z (%) 416 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}NO_6$: 416.1134; found 416.1123. HPLC-purity 91.3%.

2-(3-(2-Hydroxyphenyl)-3-oxo-1-*p*-tolylpropyl)-2*H*-indene-1,3-dione (3q): Yellow solid. Yield: 338 mg (88%). Mp 116-118 °C. IR ν_{max} (KBr, cm^{-1}): 3430 (-OH str), 3099, 2982 (aromatic C-H str), 1719, 1705 (C=O str), 1653 (aromatic, C=C str), 1452, 1325, 1215, 1131, 1026, 842. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.28 (m, 1H), 4.20 (dd, J = 12.5 Hz, 7.5 Hz, 1H), 3.76 (dd, J = 12.0 Hz, 5.0 Hz, 1H), 3.50 (d, J = 4.0 Hz, 1H), 2.17 (s, 3H), 12.07 (s, br, D_2O exchangeble, 1H), 7.92 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.86 (d, J = 8.0 Hz,1H), 7.84 (d, J = 7.5 Hz, 1H), 7.72 (m, 1H), 7.56 (m, 1H), 7.48 (m, 1H), 7.11 (d, J =

8.0 Hz, 2H), 6.94 (m, 4H). ^{13}C-NMR ($CDCl_3$, 125MHz) δ (ppm): 200.5, 200.4, 199.2 (C=O), 162.4, 142.6, 142.3, 136.9, 136.4, 135.4, 135.3, 130.0, 129.1, 128.1, 122.9, 122.8, 119.4, 119.0, 118.4, 56.9, 40.5, 39.0, 20.8. MS (ESI): m/z (%) 385 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{25}H_{20}O_4$: 385.1440; found 385.1430. HPLC-purity 93.3%.

2-(3-(2-Hydroxyphenyl)-3-oxo-1-(3,4,5-trimethoxyphenyl)propyl)-2*H*-indene-1,3-dione (3r): Yellow solid. Yield: 409.4 mg (89%). Mp 122-124 °C. IR ν_{max} (KBr, cm^{-1}): 3419 (-OH str), 3129, 2972 (aromatic C-H str), 1730, 1703 (C=O str), 1630 (aromatic, C=C str), 1588, 1499, 1453, 1255, 1123, 999, 764. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.25 (m, 1H), 4.14 (dd, J = 13.5 Hz, 8.0 Hz, 1H), 4.00 (d, J = 8.5 Hz, 1H), 3.74 (s, 6H), 3.69 (s, 3H), 3.48 (d, J = 7.0 Hz, 1H), 12.07 (s, br, D_2O exchangeble, 1H), 7.93 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 7.87 (m, 1H), 7.82 (m, 1H), 7.74 (m, 2H), 7.48 (t, 1H), 6.95 (m, 2H), 6.45 (s, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 204.3, 200.6, 199.3 (C=O), 162.4, 152.9, 142.6, 142.3, 136.8, 136.6, 135.7, 135.5, 135.5, 129.9, 123.0, 122.7, 119.3, 119.0, 118.5, 60.6, 56.9, 56.0, 40.4, 39.9. MS (ESI): m/z (%) 461 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{27}H_{24}O_7$: 461.1600; found 461.1583. HPLC-purity 92.6%.

2-(3-(2-Aminophenyl)-1-(4-chlorophenyl)-3-oxopropyl)-2*H*-indene-1,3-dione (3s): Yellow solid. Yield: 343.4 mg (85%). Mp 185-187 °C. IR ν_{max} (KBr, cm^{-1}): 3447 (-NH_2 str), 3337, 3162 (aromatic C-H str), 1735, 1705 (C=O str), 1618 (aromatic, C=C str), 1587, 1489, 1402, 1255, 1165, 1013, 743. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.29 (m, 1H), 4.11 (dd, J = 12.5 Hz, 7.0 Hz, 1H), 3.58 (dd, J = 12.5 Hz, 5.0 Hz, 1H), 3.51 (d, J = 6.5 Hz, 1H), 6.19 (s, br, D_2O exchangeble, 2H), 7.86 (m, 3H), 7.73 (m, 2H), 7.26 (m, 1H), 7.21 (d, J = 8.5 Hz, 2H), 7.10 (dd, J = 7.0 Hz, 2.0 Hz, 2H), 6.68 (m, 1H), 6.65 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.2, 199.9, 199.3 (C=O), 150.4, 142.5, 142.2, 139.1, 135.5, 134.5, 132.7, 131.0, 129.8, 128.5, 122.7, 122.8, 117.8, 117.3, 115.9, 57.0, 40.9, 39.1. MS (ESI): m/z (%) 404 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{24}H_{18}ClNO_3$: 404.1053; found 404.1046. HPLC-purity 91.5%.

2-(3-(2-Aminophenyl)-3-oxo-1-*p*-tolylpropyl)-2*H*-indene-1,3-dione (3t): Yellow solid. Yield: 318 mg (83%). Mp 120.122 °C. IR ν_{max} (KBr, cm^{-1}): 3446, 3336 (-NH_2 str), 3152 (aromatic C-H str), 1726, 1705 (C=O str), 1613 (aromatic, C=C str), 1586, 1401, 1254, 1201, 1159, 1022, 749. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.28 (m, 1H), 4.11 (dd, J = 13.0 Hz, 7.0 Hz, 1H), 3.55 (m, 2H), 2.18 (s, 3H), 6.21 (s, br, D_2O exchangeble, 2H), 7.87 (m, 3H), 7.70 (m, 2H), 7.25 (m, 2H), 7.14 (m, 1H), 6.94 (m, 2H), 6.66 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.6, 200.5, 199.7, (C=O), 150.4, 142.7, 142.3, 137.6, 136.4, 135.2, 134.3, 131.1, 129.0, 128.2, 122.9, 122.7, 117.9, 117.3, 115.8, 57.2, 41.1, 39.4, 20.8. MS (ESI): m/z (%): 384 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{25}H_{21}NO_3$: 384.1600; found 384.1588. HPLC-purity 90.0%.

2-(3-(2-Aminophenyl)-1-(3-nitrophenyl)-3-oxopropyl)-2*H*-indene-1,3-dione (3u): Yellow solid. Yield: 306 mg (80%). Mp 152-154 °C. IR ν_{max} (KBr, cm^{-1}): 3421, 3298 ($-NH_2$ str), 3059 (aromatic C-H str), 1733, 1713 (C=O str), 1613 (aromatic, C=C str), 1543, 1415, 1322, 1202, 1121, 998, 742. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.36 (m, 1H), 4.03 (dd, *J* = 13.0 Hz, 7.0 Hz, 1H), 3.59 (dd, *J* = 13.5 Hz, 6.0 Hz, 1H), 3.48 (d, *J* = 7.5 Hz, 1H), 6.08 (s, br, D_2O exchangeble, 2H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.82 (m, 1H), 7.77 (d, *J* = 7.5 Hz, 2H), 7.67 (m, 2H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.28 (m, 1H), 7.18 (m, 1H), 6.60 (m, 1H), 6.54 (d, *J* = 8.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 200.2, 199.9, 199.5 (C=O), 150.5, 142.5, 142.3, 139.4, 136.2, 135.0, 133.1, 130.8, 129.5, 128.5, 122.7, 122.6, 117.9, 117.2, 116.0, 57.3, 40.9, 39.6. MS (ESI): m/z (%) 415 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{25}H_{21}NO_3$: 415.1294; found 415.1280. HPLC-purity 89.4%.

(b) *Synthesis of 1,2-diazepines:* A mixture of 1,5-diketone (1 mmol) and hydrazine hydrate (3 mmol) was taken in mortar. The mixture was grounded thoroughly by a pestle for 10-20 min at room temperature. TLC monitoring, the reaction mixture was worked up by adding water (10 mL) and allowed to stand for 10-15 min. The precipitate was filtered and dried under vacuum. Further purification was accomplished by silica gel column chromatography using hexane: EtOAc (2:8, v/v) as eluent. The products were obtained in excellent yields (85-96%).

(2*E*,5a*E*)-5-(4-Chlorophenyl)-3-*p*-tolyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4a): Orange solid. Yield: 370 mg (93%). Mp 218-220 °C. IR ν_{max} (KBr, cm^{-1}): 3423 (-NH str), 3166, 3121, 3017, 2930 (aromatic C-H str), 1662 (C=O str), 1573, (aromatic, C=C str), 1510, 1394, 1197, 1084, 818, 730. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.59 (dd, *J* = 5.0 Hz, 3.0 Hz, 1H), 3.37 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.07 (dd, *J* = 13.5 Hz, 3.0 Hz, 1H), 2.22 (s, 3H), 8.55 (s, br, D_2O exchangble, 1H) 7.47 (d, *J* = 7.0 Hz, 1H), 7.36 (m, 2H), 7.21 (d, *J* = 7.0 Hz, 1H), 7.15-7.09 (m, 6H), 6.97 (d, *J* = 8.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.4 (C=O), 159.4, 154.0, 140.8, 138.5, 136.3, 135.1, 133.0, 131.3, 129.1, 128.3, 127.9, 127.5, 121.7, 115.9, 111.0, 40.7, 39.7, 21.0. MS (ESI): m/z (%): 399 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{25}H_{19}ClN_2O$: 399.1264; found 399.1251.

(2*E*,5a*E*)-3-(4-Chlorophenyl)-5-(3-nitrophenyl)-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one: (4b) Orange solid. Yield: 408.5 mg (95%). Mp 235-237 °C. IR ν_{max} (KBr, cm^{-1}): 3434, 3126 (aromatic C-H str), 1681 (C=O str), 1575 (aromatic, C=C str), 1521, 1398, 1087, 1006, 827. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.70 (dd, *J* = 5.0 Hz, 2.0 Hz, 1H), 3.42 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.07 (dd, *J* = 13.5 Hz, 3.0 Hz, 1H), 8.86 (s, br, D_2O exchangeable, 1H), 7.97 (m, 1H), 7.86 (dd, *J* = 8.0 Hz, 1.5 Hz, 1H), 7.47 (m, 1H), 7.41 (m, 2H), 7.35 (m, 2H), 7.30 (m, 1H), 7.16 (m, 2H), 7.05 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.2 (C=O), 158.5, 154.5, 148.2, 145.6, 138.1, 136.7, 133.9, 132.9, 130.9, 130.0, 129.0, 128.1, 127.5, 123.3, 122.7, 122.5, 122.2, 116.4, 109.2, 40.5, 38.1. MS (ESI): m/z (%) 430[M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{16}ClN_3O_3$: 430.0958; found 430.0962.

(2*E*,5a*E*)-3-(4-Chlorophenyl)-5-phenyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4c): Orange solid. Yield: 365.8 mg (95%). Mp 230-232 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3414 (-NH str), 3084 (aromatic C-H str), 1677 (C=O str), 1559, 1542 (aromatic, C=C str), 1379, 1323, 1079, 821. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.54 (dd, *J* = 5.0 Hz, 2.0 Hz, 1H), 3.37 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.04 (dd, *J* = 13.5 Hz, 2.5 Hz, 1H), 8.83 (s, br, D_2O exchangble, 1H) 7.42 (dd, *J* = 7.0 Hz, 1.5 Hz, 1H), 7.32-7.26 (m, 2H), 7.24-7.19 (m, 3H), 7.15-7.07 (m, 5H), 7.04 (d, *J* = 7.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 190.3 (C=O), 159.4, 153.2, 141.4, 137.2, 131.9,131.4, 130.3, 129.0, 128.4, 127.9, 127.4, 127.3, 125.5, 120.7, 115.2, 109.1, 39.1, 38.4. MS (ESI): m/z (%) 385 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}ClON_2$: 385.1108; found 385.1099.

(2*E*,5a*E*)-3,5-Bis(4-chlorophenyl)-4,5-dihydroindeno [1,2-*c*][1,2]diazepin-6(1*H*)-one (4d): Orange solid. Yield: 394 mg (94%). Mp 215-217 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3428 (-NH str), 3175, 3120 (aromatic C-H str), 1673 (C=O str), 1565 (aromatic, C=C str), 1395, 1345, 1080, 810, 769. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.61 (dd, *J* = 5.0 Hz, 2.5 Hz, 1H), 3.38 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.08 (dd, *J* = 13.5 Hz, 3.0 Hz, 1H), 8.87 (s, br, D_2O exchangble, 1H) 7.52 (m, 1H), 7.35 (m, 2H), 7.28 (m, 1H), 7.17 (m, 2H), 7.10-7.05 (m, 6H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.3 (C=O), 159.7, 154.2,142.2, 138.3, 137.3, 135.5, 132.9, 132.6, 131.4, 130.1, 129.1, 129.0, 128.7, 128.5, 127.8, 127.4, 121.9, 116.1, 110.3, 40.1, 39.1. MS (ESI): m/z (%) 419 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{16}Cl_2N_2O$: 419.0718; found 419.0711.

(2*E*,5a*E*)-3-(4-Bromophenyl)-5-*p*-tolyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4e): Orange solid. Yield: 403 mg (91%). Mp 223-225 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3437 (-NH str), 3186, 3128, 3016 (aromatic C-H str), 1665 (C=O str), 1576 (aromatic, C=C str), 1517, 1397, 1335, 1097, 850. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.52 (dd, *J* = 6.0 Hz, 2.50 Hz, 1H), 3.29 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 2.99 (dd, *J* = 13.5 Hz, 3.0 Hz, 1H), 2.15 (s, 3H), 8.51 (s, br, D_2O exchangble, 1H), 7.40 (m, 1H), 7.28 (m,2), 7.23 (m, 2H), 7.12 (m, 1H), 7.02 (m, 2H), 6.96 (dd, *J* = 7.0 Hz, 1.5 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.2 (C=O), 159.3, 153.7, 140.7, 138.4, 138.1, 136.2, 135.6, 134.2, 133.9, 132.9, 131.1, 129.8, 129.0, 128.0, 127.3, 123.4, 121.7, 115.6, 111.0, 40.1, 39.5, 20.9. MS (ESI): m/z (%) 443 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{25}H_{19}BrN_2O$: 443.0759; found 443.0761.

(2*E*,5a*E*)-3-(4-Bromophenyl)-5-(3,4,5-trimethoxyphenyl)-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-

6(1*H*)-one (4f): Orange solid. Yield: 467.1 mg (90%). Mp 215-218 °C. IR ν_{max} (KBr, cm^{-1}): 3429 (-NH str), 3166, 3113 (aromatic C-H str), 1671 (C=O str), 1602, 1570 (aromatic, C=C str), 1511, 1391, 1196, 1087, 1014, 905, 847, 715. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.49 (m, 1H), 3.64 (s, 3H), 3.61 (s, 6H), 3.05 (m, 1H), 2.94 (m, 1H), 8.83 (s, br, D_2O exchangble, 1H) 7.77 (m, 1H), 7.67 (m, 2H), 7.42 (m, 2H), 7.24 (m, 2H), 7.03 (m, 1H), 6.29 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.5 (C=O), 159.7, 154.0, 139.6, 138.4, 137.9, 137.1, 135.6, 133.0, 132.0, 130.9, 129.9, 129.2, 128.6, 128.0, 121.8, 116.1, 110.5, 60.8, 56.7, 56.2, 41.2, 39.0. MS (ESI): m/z (%) 519 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{27}H_{23}BrN_2O_4$: 519.0919; found 519.092.

(2*E*,5a*E*)-5-(4-Bromophenyl)-3-phenyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4g): Orange solid. Yield: 399 mg (93%). Mp 228-230 °C. IR ν_{max} (KBr, cm^{-1}): 3441 (-NH str), 3140, 2922 (aromatic C-H str), 1669 (C=O str), 1600 (aromatic, C=C str), 1398, 1267, 1178, 1086, 1030, 758, 693. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.64 (dd, J = 5.0 Hz, 2.5 Hz, 1H), 3.39 (dd, J = 13.5 Hz, 5.0 Hz, 1H), 3.08 (dd, J = 13.5 Hz, 3.0 Hz, 1H), 8.56 (s, br, D_2O exchangble, 1H) 7.48 (d, J = 7.0 Hz, 1H), 7.34 (m, 2H), 7.28 (m, 3H), 7.22-7.10 (m, 5H), 6.99 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.3 (C=O), 159.4, 154.0, 143.8, 138.5, 138.1, 133.0, 131.3, 131.3, 130.0, 128.5, 128.1, 127.6, 126.9, 123.8, 121.8, 115.8, 110.8, 40.7, 39.6. MS (ESI): m/z (%) 429 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}BrN_2O$: 429.0603; found 429.0595.

(2*E*,5a*E*)-3-(4-Bromophenyl)-5-(4-chlorophenyl)-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4h): Orange solid. Yield: 444.5 mg (96%). Mp 227-229 °C. IR ν_{max} (KBr, cm^{-1}): 3430 (-NH str), 3128 (aromatic C-H str), 1661 (C=O str), 1576, 1521 (aromatic, C=C str), 1399, 1085,1008, 819, 724. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.60 (dd, J = 5.0 Hz, 2.5 Hz, 1H), 3.39 (dd, J = 13.5 Hz, 5.0 Hz, 1H), 3.08 (dd, J = 13.5 Hz, 2.5 Hz, 1H), 8.70 (s, br, D_2O exchangble, 1H), 7.49 (m, 1H), 7.35 (m, 2H), 7.28 (m, 2H), 7.21 (m, 1H), 7.17 (m, 2H) 7.14 (m, 2H), 7.08 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.5 (C=O), 159.0, 142.7, 138.2, 137.3, 135.5, 132.9, 131.5, 130.1, 129.4, 128.9, 128.4, 127.8, 126.3, 121.9, 120.7, 116.0, 110.2, 40.2, 39.1. MS (ESI): m/z (%) 463 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{16}BrClN_2O$: 463.0213; found 463.0205.

(2*E*,5a*E*)-3,5-Diphenyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4i): Orange solid. Yield: 337 mg (96%). Mp 158-160 °C. IR ν_{max} (KBr, cm^{-1}): 3436 (-NH str), 3120, 3020 (aromatic C-H str), 1670 (C=O str), 1572 (aromatic, C=C str), 1390, 1335, 1196, 1077, 1002, 815, 760. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.66 (dd, J = 5.0 Hz, 2.5 Hz, 1H), 3.44 (dd, J = 13.5 Hz, 5.0 Hz, 1H), 3.10 (dd, J = 13.5 Hz, 2.5 Hz, 1H), 8.80 (s, br, D_2O exchangble, 1H) 7.30 (d, J = 7.0 Hz, 1H), 7.28 (m, 4H), 7.21-7.14 (m, 7H), 7.06 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.5 (C=O), 154.4, 144.0, 139.4, 138.4, 135.4, 135.3, 133.2, 131.3, 130.1, 129.8, 128.9, 128.6, 127.8, 127.5, 126.7, 125.6, 122.9, 116.3, 110.5, 40.8, 40.0. MS (ESI): m/z (%) 351 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{18}N_2O$: 351.1457; found 351.1452.

(2*E*,5a*E*)-3-Phenyl-5-*p*-tolyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4j): Orange solid. Yield: 343 mg (94%). Mp 212-214 °C. IR ν_{max} (KBr, cm^{-1}): 3397 (-NH str), 3196, 2985 (aromatic C-H str), 1665 (C=O str), 1591 (aromatic, C=C str), 1400, 1257, 1082, 813, 760. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.58 (dd, *J* = 5.0 Hz, 2.0 Hz, 1H), 3.43 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.09 (dd, *J* = 13.5 Hz, 2.5 Hz, 1H), 2.20 (s, 3H), 8.75 (s, br, D_2O exchangble, 1H), 7.45 (dd, *J* = 6.0 Hz, 2.5 Hz, 1H), 7.30 (m, 2H), 7.23 (m, 2H), 7.20 (m, 2H), 7.17 (m, 1H), 7.13 (m, 3H), 6.96 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.3 (C=O), 160.7, 154.0, 141.0, 139.3, 138.6, 136.1, 133.1, 132.7, 131.2, 129.1, 128.5, 128.4, 127.5, 126.6, 121.7, 115.8, 111.1, 40.3, 40.0, 21.0. MS (ESI): m/z (%) 365 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{25}H_{20}N_2O$: 365.1654; found 365.1645.

(2*E*,5a*E*)-5-(4-Chlorophenyl)-3-phenyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4k): Orange solid. Yield: 365.7 mg (95%). Mp 232-234 °C. IR ν_{max} (KBr, cm^{-1}): 3424 (-NH str), 3091 (aromatic C-H str), 1675 (C=O str), 1565, 1531 (aromatic, C=C str), 1389, 1324, 1090, 817. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.55 (dd, *J* = 5.0 Hz, 2.0 Hz, 1H), 3.38 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.03 (dd, *J* = 13.5 Hz, 2.5 Hz, 1H), 8.82 (s, br, D_2O exchangble, 1H) 7.41 (dd, *J* = 7.0 Hz, 1.5 Hz, 1H), 7.39-7.24 (m, 3H), 7.23-7.18 (m, 4H), 7.14-7.06 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 190.3 (C=O), 159.5, 153.2, 141.3, 137.9, 137.2, 132.0, 131.4, 130.3, 129.0, 128.4, 128.0, 127.5, 127.3,125.5, 120.7, 115.2, 109.1, 39.1, 38.4. MS (ESI): m/z (%) 385 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}ClN_2O$: 385.1108; found 385.1114.

(2*E*,5a*E*)-5-(3-Nitrophenyl)-3-phenyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4l): Orange solid. Yield: 360.4 mg (91%). Mp 231-233 °C. IR ν_{max} (KBr, cm^{-1}): 3433 (-NH str), 3175, 3122, 3017 (aromatic C-H str), 1682 (C=O str), 1573 (aromatic, C=C str), 1510, 1394, 1333, 1197, 1085, 1004, 889, 732.^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.76 (dd, *J* = 5.0 Hz, 2.5 Hz, 1H), 3.56 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.17 (dd, *J* = 13.5 Hz, 3.0 Hz, 1H), 8.78 (s, br, D_2O exchangble, 1H), 8.06 (d, *J* = 7.0 Hz, 1H), 7.91 (m, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.49 (m, 1H), 7.41 (m, 2H), 7.37 (m, 2H), 7.30 (m, 1H), 7.28 (m, 1H), 7.24 (m, 2H), 7.17 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 192.0 (C=O), 157.0, 144.9, 138.5, 132.8, 131.9, 130.3, 129.8, 129.5, 128.6, 128.4, 127.1, 126.7, 126.2, 125.8, 123.8, 123.4, 122.7, 115.5, 111.2, 40.8, 38.9. MS (ESI): m/z (%) 396 [M+H$^+$] HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}N_3O_3$: 396.1348; found 396.1344.

(2*E*,5a*E*)-3-(4-Nitrophenyl)-5-phenyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4m): Orange solid. Yield: 364.3 mg (92%). Mp 234-236 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3456 (-NH str), 3121, 3025, 2917 (aromatic C-H str), 1691 (C=O str), 1572 (aromatic, C=C str), 1514, 1391, 1335, 1200, 1076, 1001, 816, 713. ^{1}H-NMR (CDCl$_3$, 500 MHz) δ (ppm): 4.62 (dd, J = 5.0 Hz, 2.5 Hz, 1H), 3.36 (dd, J = 13.0 Hz, 5.0 Hz, 1H), 3.03 (dd, J = 13.5 Hz, 3.0 Hz, 1H), 8.66 (s, br, D$_2$O exchangble, 1H), 8.12 (d, J=8.0 Hz, 1H), 7.92 (m, 2H), 7.77 (m, 1H), 7.73 (m, 1H), 7.43 (d, J = 7.0 Hz, 1H), 7.19 (m, 2H), 7.10 (m, 3H), 7.01 (m, 2H). ^{13}C-NMR (CDCl$_3$, 125 MHz) δ (ppm): 191.4 (C=O), 157.6, 145.1, 138.4, 132.7, 131.6, 130.1, 128.8, 128.7, 128.5, 127.6, 127.3, 125.9, 123.7, 123.3, 122.1, 115.9, 111.5, 40.8, 39.7. MS (ESI): m/z (%) 396 [M+H^{+}]. HRMS-ESI (m/z): [M+H^{+}] calcd for $C_{24}H_{17}N_3O_3$: 396.1348; found 396.1345.

(2*E*,5a*E*)-3-(4-Nitrophenyl)-5-*p*-tolyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4n): Orange solid. Yield: 377.2 mg (92%). Mp 239-241 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3419 (-NH str), 3112 (aromatic C-H str), 1690 (C=O str), 1576 (aromatic, C=C str), 1398, 1080, 997, 893, 823. ^{1}H-NMR (CDCl$_3$, 500 MHz) δ (ppm): 4.57 (dd, J = 5.0 Hz, 2.0 Hz, 1H), 3.33 (dd, J = 13.5 Hz, 5.0 Hz, 1H), 3.01 (dd, J = 13.5 Hz, 2.5 Hz, 1H), 2.10 (s, 3H), 8.71 (s, br, D$_2$O exchangble, 1H) 7.94 (m, 2H), 7.32 (m, 2H), 7.28 (m, 4H), 6.98 (m, 2H), 6.90 (m, 2H). ^{13}C-NMR (CDCl$_3$, 125 MHz) δ (ppm): 191.4 (C=O), 157.7, 147.7, 145.3, 140.8, 138.4, 136.6, 132.7, 131.5, 130.0, 129.3, 128.0, 127.4, 127.3, 123.3, 122.0, 115.9, 111.8, 40.4, 39.1, 21.0. MS (ESI): m/z (%) 410 [M+H^{+}]. HRMS-ESI (m/z): [M+H^{+}] calcd for $C_{25}H_{19}N_3O_3$: 410.1505; found 410.1502.

(2*E*,5a*E*)-5-(4-Chlorophenyl)-3-(2-hydroxyphenyl)-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4o): Orange solid. Yield: 356.9 mg (89%). Mp 212-214 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3435 (-NH str), 3128, 2979 (aromatic C-H str), 1673 (C=O str), 1613, 1571 (aromatic, C=C str), 1498, 1398, 1249, 1195, 1086, 753. ^{1}H-NMR (CDCl$_3$, 500 MHz) δ (ppm): 4.19 (dd, J = 9.0 Hz, 5.0 Hz, 1H), 3.64 (dd, J = 14.0 Hz, 9.0 Hz, 1H), 3.29 (dd, J = 14.0 Hz, 6.5 Hz, 1H), 11.83 (s, br, D$_2$O exchangble, 1H), 8.41 (s, br, D$_2$O exchangble, 1H), 7.43 (dd, J = 8.5 Hz, 2.0 Hz, 2H), 7.38 (m, 1H), 7.08 (m, 4H), 7.03 (m, 2H), 6.99 (m, 1H), 6.71 (m, 1H), 6.65 (m, 1H). ^{13}C-NMR (CDCl$_3$, 125 MHz) δ (ppm): 191.0 (C=O), 164.1, 157.9, 154.6, 139.5, 138.3, 137.3, 132.7, 132.0, 129.7, 129.4, 128.9, 128.2, 127.6, 126.1, 121.3, 119.7, 118.9, 118.0, 117.8, 40.3, 38.2. MS (ESI): m/z (%) 401 [M+H^{+}]. HRMS-ESI (m/z): [M+H^{+}] calcd for $C_{24}H_{17}ClN_2O_2$: 401.1057; found 401.1060.

(2*E*,5a*E*)-3-(2-Hydroxyphenyl)-5-(3-nitrophenyl)-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4p): Orange solid. Yield: 350 mg (85%). Mp 224-226 ^{o}C. IR ν_{max} (KBr, cm^{-1}): 3420 (-NH str), 3101, 2981 (aromatic C-H str), 1675 (C=O str), 1571 (aromatic, C=C str), 1493, 1391, 1232, 1180, 1056, 864, 782. ^{1}H-NMR (CDCl$_3$, 500 MHz) δ (ppm): 4.24 (dd, J = 13.0 Hz, 4.0 Hz, 1H), 3.52 (dd, J = 13.0 Hz, 5.0 Hz, 1H), 3.19 (dd, J = 14.0 Hz, 5.0 Hz, 1H), 11.59 (s, br, D$_2$O exchangble, 1H), 8.35 (s, br, D$_2$O exchangble, 1H), 8.10 (m, 1H), 7.83 (m, 2H), 7.41 (m, 1H), 7.27 (m, 2H), 7.11 (m, 2H), 7.03 (m, 1H), 6.95 (m, 1H), 6.73 (m, 1H), 6.60 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 190.9 (C=O), 164.1, 157.7, 153.7, 139.6, 138.2, 137.4, 133.4, 132.2, 129.6, 129.1, 128.8, 128.1, 127.7, 126.3, 125.2, 122.1, 119.8, 118.9, 117.9, 40.2, 39.2. MS (ESI): m/z (%) 412 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{24}H_{17}N_3O_4$: 412.1297; found 412.1291.

(2*E*,5a*E*)-3-(2-Hydroxyphenyl)-5-*p*-tolyl-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1*H*)-one (4q): Orange solid. Yield: 331.5 mg (87%). Mp 208-210 °C. IR ν_{max} (KBr, cm^{-1}): 3432 (-NH str), 3181, 3117, 2965 (aromatic C-H str), 1670 (C=O str), 1609, 1560 (aromatic, C=C str), 1449, 1389, 1249, 1195, 761. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.48 (dd, *J* = 5.0 Hz, 2.0 Hz, 1H), 3.60 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 2.90 (dd, *J* = 14.0 Hz, 7.0 Hz, 1H), 2.05 (s, 3H), 11.69 (s, br, D_2O exchangble, 1H), 8.52 (s, br, D_2O exchangble, 1H), 7.50 (d, *J* = 7.0 Hz, 1H), 7.34 (m, 1H), 7.28 (m, 2H), 6.99 (m, 3H), 6.83 (m, 3H), 6.63 (m, 1H), 6.45 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.9 (C=O), 164.0, 158.2, 154.8, 139.9, 138.3, 136.3, 132.6, 131.4, 129.9, 129.1, 128.2, 127.5, 127.4, 121.6, 119.7, 118.8, 117.2, 116.5, 40.5, 37.5, 20.9. MS (ESI): m/z (%) 381 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{25}H_{20}N_2O_2$: 381.1603; found 381.1595.

(2*E*,5a*E*)-3-(2-Hydroxyphenyl)-5-(3,4,5-trimethoxyphenyl)-4,5-dihydroindeno[1,2-*c*][1,2]diazepin-6(1H)-one (4r): Orange solid. Yield: 411 mg (90%). Mp 238-240 °C. IR ν_{max} (KBr, cm^{-1}): 3436 (-NH str), 3134, 2968 (aromatic C-H str), 1665 (C=O str), 1625 (aromatic, C=C str), 1524, 1399, 1089. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 4.58 (dd, *J* = 5.0 Hz, 2.5 Hz, 1H), 3.67 (s, 6H), 3.65 (s, 3H), 3.59 (dd, *J* = 13.5 Hz, 5.0 Hz, 1H), 3.07 (dd, *J* = 13.5 Hz, 2.5 Hz, 1H), 11.82 (s, br, D_2O exchangble, 1H), 8.45 (s, br, D_2O exchangble, 1H) 7.50 (d, *J* = 6.5 Hz, 1H), 7.42 (td, 1H), 7.37 (m, 1H), 7.28 (d, *J* = 7.0 Hz, 1H), 7.14 (td, 1H), 6.86 (m, 2H), 6.60 (m, 1H), 6.43 (s, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 191.4 (C=O), 162.2, 154.9, 152.5, 151.8, 140.4, 139.8, 138.5, 136.0, 133.2, 129.2, 128.4, 128.0, 127.3, 126.5, 122.3, 119.1, 118.5, 117.7, 117.3, 60.2, 56.6, 40.3, 39.8. MS (ESI): m/z (%) 457 [M+H$^+$]. HRMS-ESI (m/z): [M+H$^+$] calcd for $C_{27}H_{24}N_2O_5$: 457.1763; found 457.1755.

(c) *Synthesis of 1,2-oxazepines*: To a stirred solution of 1,5-diketone (1 mmol) in EtOH (0.5 mL) was added hydroxylamine hydrochloride (2 mmol) and aq. NaOH (1M, 2-3 mL). The reaction mixture was refluxed for 2-3 h. TLC monitoring; the reaction mixture was worked up by neutralizing with HCl (0.5M, 2-3 mL) dropwise addition, followed by water addition (10 mL). The precipitate was filtered and dried under reduced pressure. Further purification was accomplished by silica gel column chromatography using hexane: EtOAc (1:9, v/v) as eluent. The products were obtained in excellent yields (85-88%).

(2*E*,5a*E*)-3-(4-Bromophenyl)-5-*p*-tolyl-4,5-dihydroindeno[2,1-*f*][1,2]oxazepin-6-one (5a): White solid. Yield: 377.4 mg (85%). Mp 97-99 °C. IR ν_{max} (KBr, cm^{-1}): 3127, 2917 (aromatic C-H str), 1673 (C=O str), 1584, 1391, 1015, 854, 742. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 5.72 (dd, J = 10.0 Hz, 3.0 Hz, 1H), 3.73 (m, 1H), 3.32 (dd, J = 12.5 Hz, 8.5 Hz, 1H), 2.23 (s, 3H), 7.83 (dd, J = 6.0 Hz, 2.0 Hz, 1H), 7.77 (d, J = 7.0 Hz, 2H), 7.69 (m, 2H), 7.53 (dd, J = 6.0 Hz, 2.0 Hz, 1H), 7.39 (m, 1H), 7.23 (m, 1H), 7.04 (m, 2H), 6.89 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 192.7 (C=O), 158.5, 154.9, 140.3, 138.2, 132.5, 132.2, 131.9, 129.4, 128.3, 128.1, 127.1, 126.6, 125.8, 124.3, 121.9, 116.1, 109.2, 42.7, 39.6, 21.1. MS (ESI): m/z (%) 444 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{25}H_{18}BrNO_2$: 444.0599; found 444.0587.

(2*E*,5a*E*)-3-(4-Bromophenyl)-5-phenyl-4,5-dihydroindeno[2,1-*f*][1,2]oxazepin-6-one (5b): White solid. Yield: 378.4 mg (88%). Mp 104-106 °C. IR ν_{max} (KBr, cm^{-1}): 2925 (aromatic C-H str), 1685 (C=O str), 1569, 1399, 1071, 1012, 902, 827, 757. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 5.68 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 3.66 (dd, J = 12.5 Hz, 8.5 Hz, 1H), 3.24 (dd, J = 13.0 Hz, 8.0 Hz, 1H), 7.53-7.44 (m, 5H), 7.35-7.22 (m, 6H), 7.18 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 193.1 (C=O), 158.6, 155.2, 140.6, 138.4, 132.3, 132.1, 131.9, 128.8, 128.4, 128.1, 127.2, 126.8, 125.8, 124.4, 122.1, 115.9, 108.3, 42.9, 39.6. MS (ESI): m/z (%) 430 [$M+H^+$]. HRMS-ESI (m/z): [$M+H^+$] calcd for $C_{24}H_{16}BrNO_2$: 430.0443; found 430.0440.

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