Click Reaction of Epoxides with Anthranilic Acids Using Neat Grinding To Access Benzoxazepines

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Abstract: An atom-economic, efficient, rapid (5 min), and highly regioselective one-pot click reaction has been developed for the synthesis of benzo[*e*][1,4]oxazepin-5-ones in excellent yields (78–92%). The method involves epoxide ring-opening–ring-closing cascade with anthranilic acids using neat grinding at room temperature in the presence of lithium bromide as a mild catalyst. In this procedure, pure products are obtained simply by washing the reaction mixture with warm water, thus hazardous solvents, tedious workup processes, and purification steps, such as column chromatography and recrystallization, are avoided.

Key words: epoxides, anthranilic acids, click reaction, solvent-free, grinding, 4,1-benzoxazepines, cascade reactions

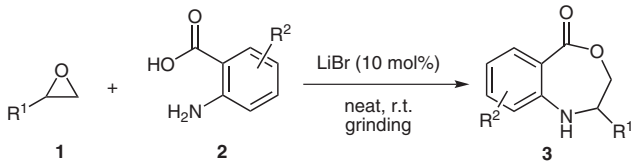
Devising a new synthetic method for a class of compounds that are not easily accessible by existing methods is an important objective in organic chemistry. In general, the chemistry of seven-membered heterocycles has been far less extensively studied than that of five- and six-membered heterocycles and the inherently strained small ring heterocycles. The synthesis of heterocycles with seven-to-eleven-membered rings is difficult for enthalpic and entropic reasons. In recent decades, the design and synthesis of seven-membered heterocycles has received much attention owing to their wide variety of applications, such as biologically active natural products,[1] drug candidates,[2] materials,[3] and catalysts.[4] Among seven-membered nitrogen heterocycles, nitrogen-containing lactones with two heteroatoms in the 1,4-positions, benzo[*e*][1,4]oxazepines, have rarely been explored. Recently, Dong and coworkers reported a nitrogen-directed ketone hydroacylation strategy for the enantioselective synthesis of this class of compounds.[5] On the other hand, numerous reports on the synthesis[6a–q] and medicinal activity[6r–v] of structural analogues of benzo[*e*][1,4]oxazepinones are available in the literature. Thus, the development of an efficient method for the synthesis of the 4,1-benzo[*e*][1,4]oxazepinone ring system appears to be an interesting target of investigation.

Recently, mechanochemical (MC) synthesis using the grinding method has received great interest and proved to be a useful laboratory technique for performing various organic reactions, for example, aldol condensations,[7] Grignard reactions,[8] Reformatsky reactions,[9] Dieckmann condensations,[10] Knoevenagel condensations,[11] reductions,[12] and others.[13] Most of these reactions are carried out at room temperature under neat conditions using only a pestle and mortar.

In recent years, annulation reactions involving three-membered heterocycles, namely epoxides and aziridines, have been used for the synthesis of medium-sized rings via the ring-opening–ring-closing cascade.[14] We have also very recently reported a rapid synthesis of benzodiazepines by an annulation reaction of aziridines with anthranilic acids.[14a]

Considering the above points and in continuation of our ongoing efforts to develop new cyclization processes,[15] we herein report the first efficient one-pot regioselective protocol for the synthesis of benzo[*e*][1,4]oxazepin-5-ones employing the click reaction of epoxides with anthranilic acids using simple grinding with a pestle and mortar under neat conditions at room temperature.

Intrigued by the inherent ring strain associated with epoxides and their synthetically important ring-opening reactions with various nucleophiles,[16] we hypothesized the synthesis of benzo[*e*][1,4]oxazepin-5-ones **3** from terminal epoxides **1** and anthranilic acids **2** via ring-opening–ring-closing cascade which could be achieved in the presence of 10 mol% of lithium bromide under neat conditions at room temperature as depicted in Scheme 1.



Scheme 1 Ring expansion of epoxides to benzo[*e*][1,4]oxazepin-5-ones

Lewis acids have been recorded as mild and efficient catalysts for epoxide activation towards nucleophilic attack.[17] Moreover, an increase in the concentration of the reactants generally enhances synthetic efficiency. Thus, to realize our hypothesis, we relied on the reaction under neat conditions using a Lewis acid, which would efficiently catalyze both the steps of epoxide ring-opening–ring-closing cascade with an anthranilic acid. We focused our initial effort on the screening of a range of Lewis acid catalysts for the synthesis of benzo[*e*][1,4]oxazepin-5-one **3a** using epoxide **1a** and anthranilic acid (**2a**) as model substrates under neat conditions (Table 1). Among the cata-

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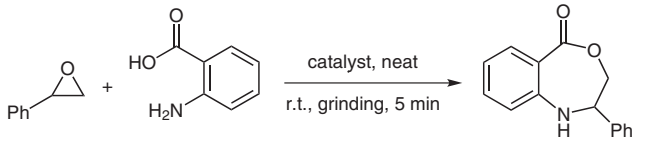
lysts tested, lithium bromide was found to be the best for the epoxide ring expansion to afford **3a** (entry 2). No appreciable amount of product **3a** was formed from **1a** and anthranilic acid (**2a**) in the absence of lithium bromide after grinding for 5 minutes at room temperature, demonstrating its catalytic efficiency. This is in accordance with the strong oxophilicity of Li^+ in the activation of oxygen-containing electrophiles to nucleophilic attack.[17a,c]

Table 1 Optimization of the Catalyst in the Synthesis of Benzo[*e*][1,4]oxazepin-5-one **3a**[a]



1a **2a** **3a**

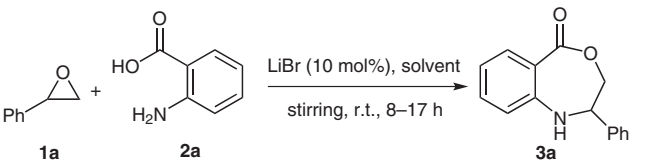
Entry	Catalyst	mol%	Yield[b] (%)
1	LiCl	10	69
2	LiBr	10	87
3	LiBr	5	78
4	LiBr	15	87
5	LiI	10	65[c]
6	NaCl	10	24
7	NaBr	10	30
8	$AlCl_3$	10	60
9	$AlBr_3$	10	62
10	$FeCl_3$	10	53
11	$FeBr_3$	10	57
12	$CuCl_2$	10	35
13	$CuBr_2$	10	39

[a] Reaction conditions: epoxide **1a** (1 mmol), anthranilic acid (**2a**, 1 mmol), Lewis acid (5–15 mol%), grinding, r.t., 5 min.
[b] Isolated yield of purified product **3a**.
[c] In addition to **3a** (65%), 2-iodo-2-phenyl-*N*-tosylethylamine was also isolated in 26% yield.

For comparison purposes, the reaction was also performed in different solvents using lithium bromide as the catalyst, but significantly lower yields of **3a** were obtained with relatively longer reaction times of 8–17 hours (Table 2). Of the solvents tested, the best solvent in terms of yield and reaction time was water (entry 1). With the optimal conditions established, the grinding method permits us to introduce great molecular diversity, including substitution and scaffold diversity, under mild reaction conditions.

A large number of benzo[*e*][1,4]oxazepin-5-ones **3** were synthesized rapidly and in excellent yields with complete regioselectivity; the results are summarized in Table 3. The regioselectivity of the reaction was ascertained by recording the ^{1}H NMR spectra of the crude sample, and we

Table 2 Comparison of Solvents in the Synthesis of Benzo[*e*][1,4]oxazepin-5-one **3a**[a]



1a **2a** **3a**

Entry	Solvent	Time (h)	Yield[b] (%)
1	H_2O	8	83
2	THF	14	75
3	1,4-dioxane	15	77
4	EtOH	11	73
5	CH_2Cl_2	11	78
6	$CHCl_3$	11	74
7	toluene	17	67

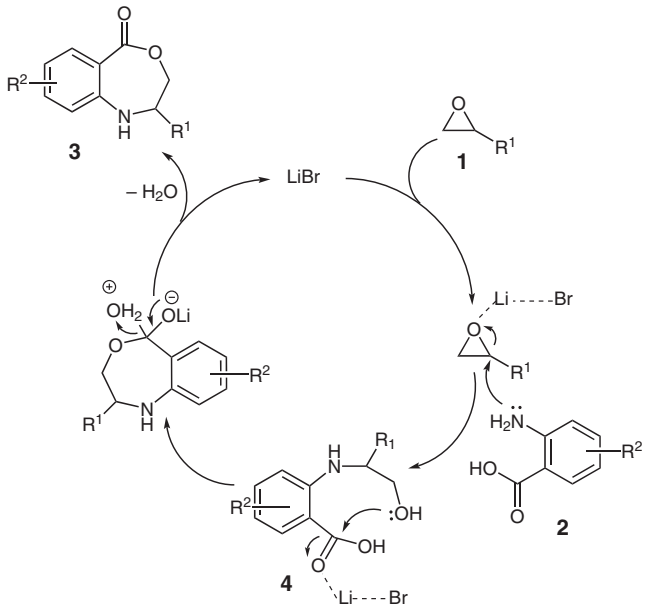
[a] Reaction conditions: epoxide **1a** (1 mmol), anthranilic acid (**2a**, 1 mmol), LiBr (10 mol%), solvent (1 mL), r.t.
[b] Isolated yield of purified product **3a**.

found that the regioisomer **3** was formed exclusively. This is in conformity with the earlier observations that in the case of aryl epoxides, the ring opening occurs at the 2-position.[17c,d] The reaction is straightforward and works well for various epoxides bearing both electron-donating and electron-withdrawing groups (Table 3). Anthranilic acids **2** bearing an electron-withdrawing group give slightly lower yields (entries 5–8) than those bearing electron-donating groups (entries 9–12).

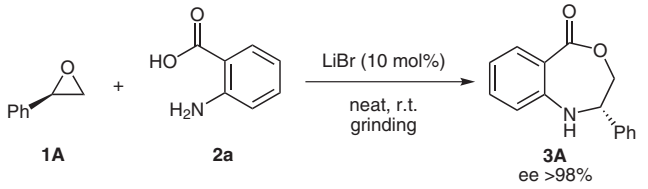
On the basis of the above experimental results, a plausible mechanism for the formation of benzo[*e*][1,4]oxazepin-5-ones **3** is depicted in Scheme 2. Anthranilic acid **2** contains two nucleophilic centers, the amino group and the carboxy group. Under neutral conditions the nucleophilic properties of the amino group dominate.[18] Lithium bromide activates the epoxide ring through coordinating with its oxygen, which facilitates regioselective nucleophilic epoxide opening with the amino group of anthranilic acid **2** to form intermediate **4**. Intramolecular dehydrative cyclization of **4** affords benzo[*e*][1,4]oxazepin-5-ones **3** and liberates lithium bromide to complete the catalytic cycle (Scheme 2).

In a pilot work on the one-pot synthesis of benzo[*e*][1,4]oxazepin-5-one **3A** (Scheme 3), a mixture of (*R*)-epoxide **1A** (1 mmol), anthranilic acid (**2a**, 1 mmol), and lithium bromide (10 mol%) was subjected to grinding in a mortar with a pestle at room temperature for five minutes to afford (*S*)-benzo[*e*][1,4]oxazepin-5-one **3A** in 91% yield with >98% ee as determined by chiral HPLC [chiral Eurocel column (250 × 4.6 mm, 5μ), λ = 225 nm, *i*-PrOH–hexane, 10:90, 1 mL/min): t_R = 3.8 (major), 5.7 min (minor)]; specific rotation $[\alpha]_D^{20}$ –135 (*c* 0.90, THF). This shows that the ring opening of optically active (*R*)-epox-

ide **1A** with anthranilic acid **2a** proceeds via an S_N2-type pathway.



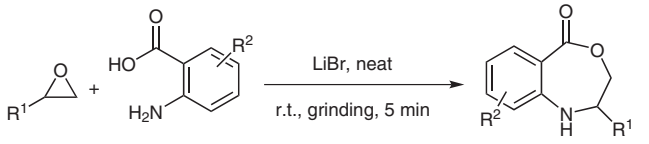
Scheme 2 A plausible mechanism and catalytic cycle of ring expansion of epoxides



Scheme 3 Synthesis of (*S*)-2-phenyl-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (**3A**)

In summary, we have demonstrated a highly efficient one-pot click reaction of epoxides with anthranilic acids for the synthesis of relatively less explored benzo[*e*][1,4]oxazepin-5-one derivatives. This rapid (5 min) synthesis is performed at room temperature under neat conditions using simple grinding. The pure products are obtained simply by washing the reaction mixture with warm water. Thus tedious workup and purification steps, such as column chromatography and recrystallization, are avoided. Moreover, atom-economy, economic viability of the catalyst, high yield, and formation of water as the sole byproduct are additional advantages of the present methodology, which make it one of the most convenient, efficient, and inexpensive methodologies for the synthesis of this class of compounds.

Table 3 Synthesis of Benzo[*e*][1,4]oxazepin-5-ones **3**[a]



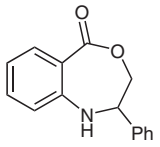
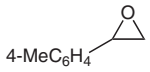
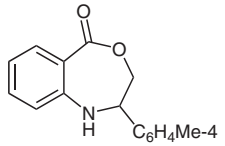
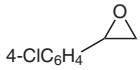
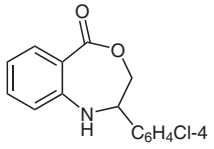
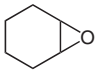
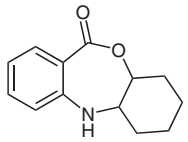
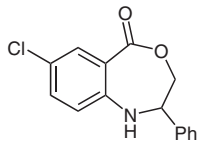
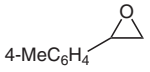
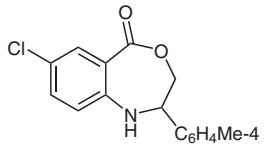
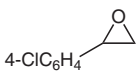
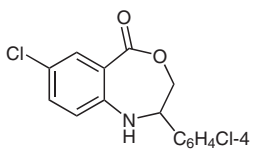
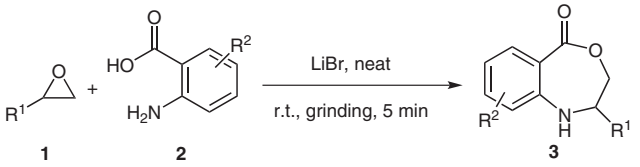
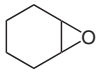
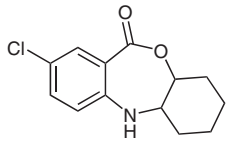
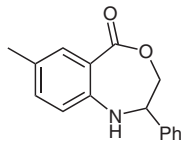
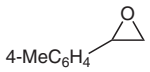
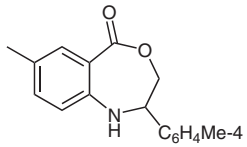
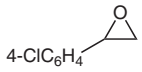
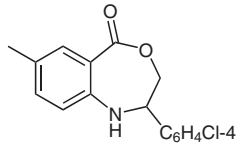
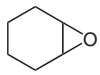
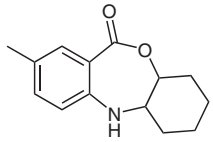
Entry	Epoxide **1**	R^2	Product **3**	Yield[b,c] (%)
1		H	 **3a**	87
2		H	 **3b**	90
3		H	 **3c**	91
4		H	 **3d**	82
5		5-Cl	 **3e**	85
6		5-Cl	 **3f**	89
7		5-Cl	 **3g**	88

Table 3 Synthesis of Benzo[*e*][1,4]oxazepin-5-ones **3**[a] (continued)



1 **2** **3**

Entry	Epoxide **1**	R^2	Product **3**	Yield[b,c] (%)
8		5-Cl	 **3h**	78
9		5-Me	 **3i**	86
10		5-Me	 **3j**	92
11		5-Me	 **3k**	89
12		5-Me	 **3l**	84

[a] Reaction conditions: epoxide **1** (1 mmol), anthranilic acid **2a** (1 mmol), LiBr (10 mol%), grinding, r.t., 5 min.
[b] Isolated yield of purified product **3**.
[c] All compounds are solid, gave C, H, and N analyses within ±0.36%, and satisfactory spectral (IR, ^{1}H NMR, ^{13}C NMR, and EIMS) data.

Melting points were determined by open glass capillary method and are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer 993 IR spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker Avance II (400 MHz) FT spectrometer in DMSO-d_6 using TMS as internal reference. ^{13}C NMR spectra were recorded on the same instrument at 100 MHz in DMSO-d_6 and TMS was used as internal reference. Mass (EI) spectra were recorded on Jeol D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic C, H, and N analyzer. All chemicals used were reagent grade and were used as received without further purification. Silica gel-G was used for TLC.

Benzo[*e*][1,4]oxazepin-5-ones 3 by One-Pot Synthesis Using Neat Grinding; General Procedure

Epoxide **1** (1 mmol), anthranilic acid **2** (1 mmol), and LiBr (10 mol%) were thoroughly ground in a mortar with a pestle for 5 min at r.t. After completion of the reaction (TLC monitoring, EtOAc–hexane, 2:3), the mixture was washed with warm H_2O to afford an analytically pure sample of benzo[*e*][1,4]oxazepin-5-one **3** (Table 3).

2-Phenyl-2,3-dihydrobenzo[*e*][1,4]oxazepin-5-one (3a): One-Pot Synthesis in the Solution Phase; General Procedure

A mixture of epoxide **1a** (1 mmol), anthranilic acid (**2a**, 1 mmol), and LiBr (10 mol%) in solvent (1 mL) was stirred at r.t. for the time indicated in Table 2. After completion of the reaction (TLC monitoring, EtOAc–hexane, 2:3), the crude product was filtered and washed with warm H_2O to afford an analytically pure sample of 4,1-benzoxazepin-5-one **3a**.

2-Phenyl-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3a)

Yellow solid; yield: 207 mg (87%); mp 172–175 °C.

IR (KBr): 695, 745, 1582, 1602, 1720, 3325 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.63 (dd, *J* = 10.8, 7.1 Hz, 1 H), 3.78 (dd, *J* = 10.8, 5.6 Hz, 1 H), 4.52 (dd, *J* = 7.1, 5.6 Hz, 1 H), 5.01 (br, 1 H, NH, exchanged with D_2O), 6.41 (dd, *J* = 8.4, 1.4 Hz, 1 H), 6.50 (m, 1 H), 7.10–7.35 (m, 5 H), 7.82 (m, 1 H), 8.57 (dd, *J* = 8.4, 1.4 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 60.1, 77.6, 109.1, 116.4, 117.8, 126.6, 127.4, 128.5, 130.2, 132.8, 139.1, 147.6, 168.2.

MS (EI): *m*/*z* = 239 (M$^+$).

Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.62; H, 5.13; N, 5.68.

2-(4-Methylphenyl)-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3b)

Yellow solid; yield: 227 mg (90%); mp 146–147 °C.

IR (KBr): 825, 1578, 1598, 1724, 3332 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.34 (s, 3 H), 3.60 (dd, *J* = 10.6, 7.2 Hz, 1 H), 3.76 (dd, *J* = 10.6, 5.4 Hz, 1 H), 4.50 (dd, *J* = 7.2, 5.4 Hz, 1 H), 4.98 (br, 1 H, NH, exchanged with D_2O), 6.39 (dd, *J* = 8.3, 1.3 Hz, 1 H), 6.50 (m, 1 H), 7.05–7.36 (m, 4 H), 7.80 (m, 1 H), 8.56 (dd, *J* = 8.3, 1.3 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 25.1, 60.3, 77.5, 109.4, 115.9, 118.2, 127.6, 128.1, 130.5, 132.2, 135.3, 138.1, 147.8, 168.5.

MS (EI): *m*/*z* = 253 (M$^+$).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.50; H, 6.20; N, 5.88.

2-(4-Chlorophenyl)-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3c)

White solid,; yield: 248 mg (91%); mp 191–193 °C.

IR (KBr): 830, 1576, 1603, 1718, 3328 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.65 (dd, *J* = 10.9, 7.3 Hz, 1 H), 3.79 (dd, *J* = 10.9, 5.5 Hz, 1 H), 4.55 (dd, *J* = 7.3, 5.5 Hz, 1 H), 5.06 (br, 1 H, NH, exchanged with D_2O), 6.42 (dd, *J* = 8.4, 1.5 Hz, 1 H), 6.52 (m, 1 H), 7.64–7.68 (m, 2 H), 7.84 (m, 1 H), 8.10–8.16 (m, 2 H), 8.59 (dd, *J* = 8.4, 1.5 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 60.9, 77.2, 110.1, 116.2, 118.4, 127.8, 128.6, 130.5, 132.4, 133.3, 139.2, 147.7, 168.3.

MS (EI): *m*/*z* = 273 (M$^+$).

Anal. Calcd for $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42; N, 5.12. Found: C, 65.51; H, 4.61; N, 5.33.

5a,6,7,8,9,9a-Hexahydrodibenzo[*b*,*e*][1,4]oxazepin-11(5*H*)-one (3d)

Yellow solid; yield: 177 mg (82%); mp 78–79 °C.

IR (KBr): 1450, 1580, 1604, 1722, 2910, 3332 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.30–1.67 (m, 4 H), 1.79–1.84 (m, 1 H), 2.05–2.15 (m, 2 H), 2.19–2.27 (m, 1 H), 3.12–3.24 (ddd, *J* = 11.5, 11.2, 3.1 Hz, 1 H), 3.86–3.88 (ddd, *J* = 11.3, 11.2, 3.1 Hz, 1 H), 5.01 (br, 1 H, NH, exchanged with D_2O), 6.41 (dd, *J* = 8.4, 1.4 Hz, 1 H), 6.50 (m, 1 H), 7.81 (m, 1 H), 8.54 (dd, *J* = 8.4, 1.4 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.7, 22.9, 27.6, 28.5, 56.1, 85.8, 108.8, 115.9, 118.2, 130.1, 132.6, 147.6, 168.2.

MS (EI): *m*/*z* = 217 (M^+).

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.72; H, 6.66; N, 6.73.

7-Chloro-2-phenyl-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3e)
Yellow solid; yield: 232 mg (85%); mp 181–182 °C.

IR (KBr): 692, 747, 1458, 1576, 1598, 1718, 3335 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.64 (dd, *J* = 10.9, 7.3 Hz, 1 H), 3.80 (dd, *J* = 10.9, 5.6 Hz, 1 H), 4.53 (dd, *J* = 7.3, 5.6 Hz, 1 H), 5.04 (br, 1 H, NH, exchanged with D_2O), 6.76 (dd, *J* = 8.5, 1.3 Hz, 1 H), 7.12–7.36 (m, 5 H), 7.95 (m, 1 H), 8.69 (dd, *J* = 8.5, 1.3 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 60.1, 77.5, 109.1, 115.4, 123.8, 126.8, 127.5, 128.7, 130.2, 133.1, 139.5, 147.4, 168.3.

MS (EI): *m*/*z* = 273 (M^+).

Anal. Calcd for $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42; N, 5.12. Found: C, 65.70; H, 4.61; N, 5.44.

7-Chloro-2-(4-methylphenyl)-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3f)
Yellow solid; yield: 255 mg (89%); mp 153–155 °C.

IR (KBr): 840, 1454, 1582, 1596, 1720, 3328 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.33 (s, 3 H), 3.62 (dd, *J* = 10.8, 7.1 Hz, 1 H), 3.79 (dd, *J* = 10.8, 5.5 Hz, 1 H), 4.51 (dd, *J* = 7.1, 5.5 Hz, 1 H), 5.00 (br, 1 H, NH, exchanged with D_2O), 6.72 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.03–7.31 (m, 4 H), 7.94 (m, 1 H), 8.66 (dd, *J* = 8.4, 1.4 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 25.7, 60.4, 77.2, 109.3, 115.5, 123.5, 126.9, 128.7, 130.5, 133.4, 135.8, 139.2, 147.1, 168.

MS (EI): *m*/*z* = 287.07 (M^+).

Anal. Calcd for $C_{16}H_{14}ClNO_2$: C, 66.79; H, 4.90; N, 4.87. Found: C, 66.95; H, 4.63; N, 5.12.

7-Chloro-2-(4-chlorophenyl)-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3g)
White solid; yield: 270 mg (88%); mp 206–208 °C.

IR (KBr): 846, 1452, 1577, 1598, 1722, 3326 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 3.67 (dd, *J* = 10.8, 7.2 Hz, 1 H), 3.81 (dd, *J* = 10.8, 5.7 Hz, 1 H), 4.55 (dd, *J* = 7.2, 5.7 Hz, 1 H), 5.08 (br, 1 H, NH, exchanged with D_2O), 6.77 (dd, *J* = 8.5, 1.3 Hz, 1 H), 7.65–7.69 (m, 2 H), 7.96 (m, 1 H), 8.12–8.19 (m, 2 H), 8.67 (dd, *J* = 8.5, 1.3 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 60.3, 77.5, 109.6, 115.2, 123.8, 126.7, 128.9, 130.2, 131.8, 133.2, 139.6, 147.4, 168.2.

MS (EI): *m*/*z* = 307 (M^+).

Anal. Calcd for $C_{15}H_{11}Cl_2NO_2$: C, 58.46; H, 3.60; N, 4.55. Found: C, 58.23; H, 3.92; N, 4.67.

2-Chloro-5a,6,7,8,9,9a-hexahydrodibenzo[*b*,*e*][1,4]oxazepin-11(5*H*)-one (3h)
Yellow solid; yield: 195 mg (78%); mp 89–91 °C.

IR (KBr): 1452, 1455, 1582, 1605, 1724, 2908, 3332 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.31–1.69 (m, 4 H), 1.82–1.88 (m, 1 H), 2.08–2.18 (m, 2 H), 2.23–2.30 (m, 1 H), 3.14–3.27 (ddd, *J* = 11.6, 11.4, 3.5 Hz, 1 H), 3.87–3.89 (ddd, *J* = 11.4, 11.2, 3.2 Hz, 1 H), 5.04 (br, 1 H, NH, exchanged with D_2O), 6.76 (dd, *J* = 8.4, 1.3 Hz, 1 H), 7.96 (m, 1 H), 8.67 (dd, *J* = 8.4, 1.3 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.5, 22.7, 27.2, 28.8, 56.5, 85.6, 108.2, 116.1, 122.5, 130.4, 133.1, 147.1, 168.3.

MS (EI): *m*/*z* = 251 (M^+).

Anal. Calcd for $C_{13}H_{14}ClNO_2$: C, 62.03; H, 5.61; N, 5.56. Found: C, 62.19; H, 5.31; N, 5.34.

7-Methyl-2-phenyl-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3i)
White solid; yield: 217 mg (86%); mp 164–165 °C.

IR (KBr): 705, 745, 1452, 1580, 1605, 1718, 3320 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.32 (s, 3 H), 3.60 (dd, *J* = 10.7, 7.2 Hz, 1 H), 3.76 (dd, *J* = 10.7, 5.6 Hz, 1 H), 4.50 (dd, *J* = 7.2, 5.6 Hz, 1 H), 5.00 (br, 1 H, NH, exchanged with D_2O), 6.72 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.11–7.35 (m, 5 H), 7.89 (m, 1 H), 8.61 (dd, *J* = 8.4, 1.4 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 25.3, 60.3, 77.8, 109.3, 116.7, 126.2, 126.9, 127.7, 128.9, 130.8, 133.3, 139.4, 147.2, 168.5.

MS (EI): *m*/*z* = 253 (M^+).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.65; H, 6.18; N, 5.33.

7-Methyl-2-(4-methylphenyl)-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3j)
White solid; yield: 245 mg (92%); mp 132–133 °C.

IR (KBr): 1603, 815, 1582, 1721, 3342 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.33 (s, 3 H), 2.36 (s, 3 H), 3.61 (dd, *J* = 10.6, 7.2 Hz, 1 H), 3.75 (dd, *J* = 10.6, 5.7 Hz, 1 H), 4.52 (dd, *J* = 7.2, 5.7 Hz, 1 H), 5.03 (br, 1 H, NH, exchanged with D_2O), 6.70 (dd, *J* = 8.3, 1.4 Hz, 1 H), 7.05–7.34 (m, 4 H), 7.88 (m, 1 H), 8.59 (dd, *J* = 8.3, 1.4 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 25.3, 25.8, 60.5, 77.2, 109.1, 116.2, 126.2, 127.5, 128.8, 130.8, 132.4, 135.1, 138.3, 147.5, 168.2.

MS (EI): *m*/*z* = 267 (M^+).

Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.69; H, 6.24; N, 5.53.

2-(4-Chlorophenyl)-7-methyl-2,3-dihydrobenzo[*e*][1,4]oxazepin-5(1*H*)-one (3k)
Yellow solid; yield: 255 mg (89%); mp 183–185 °C.

IR (KBr): 850, 1442, 1582, 1602, 1718, 3332 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.34 (s, 3 H), 3.63 (dd, *J* = 10.6, 7.4 Hz, 1 H), 3.78 (dd, *J* = 10.6, 5.5 Hz, 1 H), 4.53 (dd, *J* = 7.4, 5.5 Hz, 1 H), 5.07 (br, 1 H, NH, exchanged with D_2O), 6.71 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.67–7.70 (m, 2 H), 7.89 (m, 1 H), 8.13–8.21 (m, 2 H), 8.65 (dd, *J* = 8.4, 1.4 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 25.4, 60.7, 77.4, 109.7, 115.7, 126.4, 127.5, 128.3, 131.1, 132.2, 133.5, 139.6, 147.5, 168.1.

MS (EI): *m*/*z* = 287 (M^+).

Anal. Calcd for $C_{16}H_{14}ClNO_2$: C, 66.79; H, 4.90; N, 4.87. Found: C, 67.09; H, 4.99; N, 4.54.

2-Methyl-5a,6,7,8,9,9a-hexahydrodibenzo[*b*,*e*][1,4]oxazepin-11(5*H*)-one (3l)
Yellow solid; yield: 194 mg (84%); mp 83–84 °C.

IR (KBr): 1450, 1578, 1604, 1722, 2875, 3315 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.31–1.68 (m, 4 H), 1.80–1.85 (m, 1 H), 2.06–2.16 (m, 2 H), 2.21–2.29 (m, 1 H), 2.34 (s, 3 H), 3.12–3.26 (ddd, *J* = 11.5, 11.4, 3.6 Hz, 1 H), 3.85–3.87 (ddd, *J* =

11.4, 11.3, 3.3 Hz, 1 H), 5.02 (br, 1 H, NH, exchanged with D_2O), 6.72 (dd, J = 8.4, 1.4 Hz, 1 H), 7.87 (m, 1 H), 8.65 (dd, J = 8.4, 1.3 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.5, 22.8, 25.2, 27.8, 28.7, 56.3, 85.4, 108.5, 116.1, 126.1, 130.8, 133.4, 147.3, 168.4.

MS (EI): m/z = 231 (M^+).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.99; H, 7.28; N, 6.37.

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