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# Dibenzo[*b*,*e*]azepin-6-ones and Seven-Membered Sultam Derivatives: Convenient Synthesis via Palladium-Catalyzed Regioselective Intramolecular Heck Reaction and Application towards Drug-Like Small Molecules

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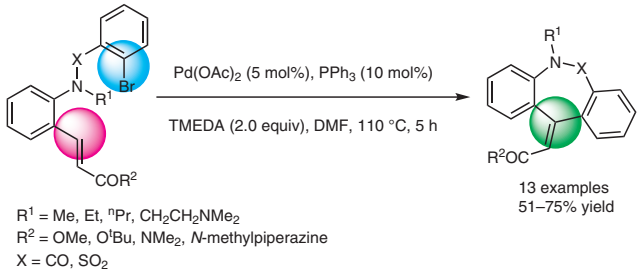


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**Abstract** A new, convenient synthesis of dibenzo[*b*,*e*]azepin-6-ones and seven-membered sultam derivatives have been envisaged via Pd-catalyzed regioselective intramolecular Heck reaction of the corresponding easily accessible precursors. This protocol has been successfully implemented to synthesize *N*-methyldarenzepine in four steps and in good yield. Moreover, one of the intermediates has been utilized for the synthesis of a new analogue of darenzepine. Preliminary modeling studies were performed to investigate the binding potential to muscarinic acetylcholine receptor (M4).

**Key words** intramolecular Heck reaction, regioselectivity, dibenzo[*b*,*e*]azepin-6-ones, seven-membered sultams, docking, M4 receptor

Dibenzoazepinones are tricyclic lactams possessing a seven-membered amide ring fused with benzene ring on both sides. Being the privileged core and identified in many alkaloids and pharmaceutically relevant organic molecules, dibenzoazepinones have attracted much significance in organic synthesis.[1] Amongst this class of compounds, dibenzo[*b*,*e*]azepin-6-one ring systems in particular, has been the subject of considerable research mainly due to their wide range of pharmacological properties such as antiulcer agent darenzepine (**A**),[2] anticonvulsant drug (**B**),[3] $\alpha_v\beta_3$ antagonist (**C**),[4] and liver X receptor (LXR)-mediated transrepressional and transactivational activities (**D**),[5] etc. (Figure 1). Very recent reports also showed that darenzepine, mediated through co-activation of the M1 and M4 muscarinic acetylcholine receptors, may be therapeutically beneficial for the treatment of schizophrenia and Alzheimer's diseases.[6] As stated above, N-substituted dibenzoazepinone scaffold has also been successfully employed in the synthesis of new integrin $\alpha_v\beta_3$ antagonists.[4] Moreover, dibenzo[*b*,*e*]azepine systems are known to exhibit potent central nervous system (CNS) activity such as neuroleptic and anticholinergic activities.[7]

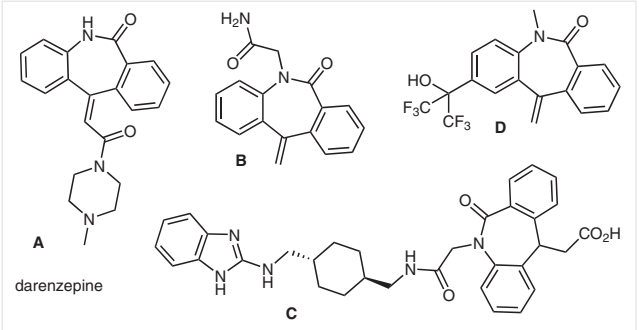
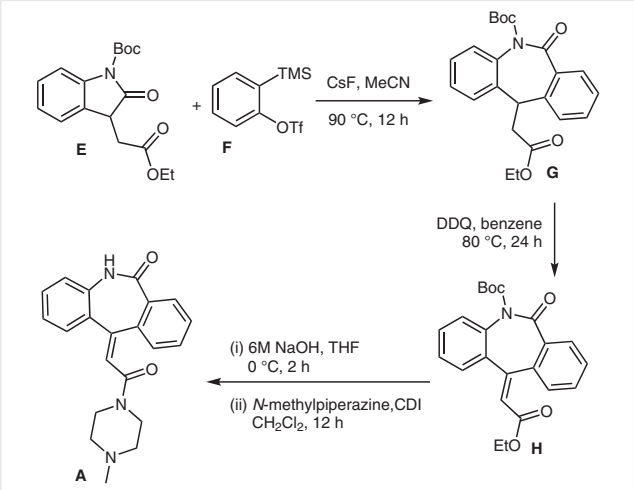



**Figure 1** Some bioactive dibenzoazepinones

Despite the widespread importance, methods to prepare the dibenzo[*b*,*e*]azepin-6-one skeletons such as dibenzo[*b*,*e*]azepin-11-ylidene]acetic acid scaffolds per se, are scarce though. For example, dibenzoazepinone derivatives were synthesized via Schmidt rearrangement followed by Wittig–Horner olefination reactions,[4] tandem reduction-lactamization sequence,[8] and regio- and chemoselective direct benzylation reaction.[9] Recently, Mehta and co-workers[10] have reported the synthesis of darenzepine (**A**), an antiulcer agent and a scaffold of dibenzo[*b*,*e*]azepin-6-one series via temperature controlled aryne insertion cascade reaction on substituted oxindole (Scheme 1). Besides, syntheses of benzazepines are also reported.[11]



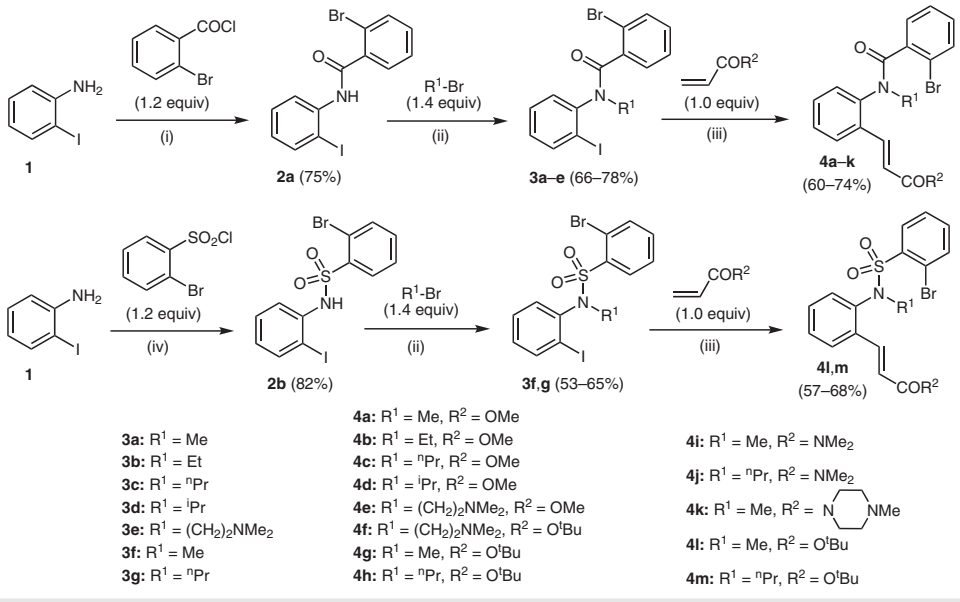

**Scheme 1** Recent report on the synthesis of darenzepine

Moreover, sultams, in particular fused biaryl sultams, have also emerged as privileged structures in drug discovery because of their diverse enzyme inhibitory activity and active role in selective serotonin reuptake inhibition.[12–14]

Several methods for the synthesis of sultam derivatives were reported.[15] But, biaryls that are fused to a seven-membered sultam have been synthesized with limited success. These include Friedel–Crafts reactions,[16] intramolecular direct C–H arylations,[17] intramolecular oxidative coupling reactions[18] and carbometalation.[19]

The search for a new and more convenient strategy to construct dibenzo[*b*,*e*]azepin-6-ones and seven-membered sultam analogues thus remains to be attractive. Palladium-catalyzed reactions are very powerful and useful tools for the construction of carbon–carbon and carbon–heteroatom bonds[20] due to their efficient catalytic activities on the reaction and having no interference properties towards a wide range of functional groups present in the substrate molecules. Moreover, most of the palladium-catalyzed reactions, particularly the Heck reaction, proceeds via a stereo- and regioselective pathway. These advantages have led to significant growth on the Heck methodologies for the syntheses of heterocyclic compounds of various ring sizes.[21–26] Thus, dibenzoazepinones and biaryls fused to a seven-membered sultam have been synthesized by means of palladium-catalyzed intramolecular Heck/reductive Heck strategies where either tributylvinyltin or 2,4,6-trivinylcyclotriboroxane or tosyl chloride or phenylacetylene were used as alkene/alkyne substrates in the initial step.[5,27–29] These observations prompted further investigation towards identification of general methodology employing intramolecular Heck reaction as the key step for the synthesis of dibenzo[*b*,*e*]azepin-6-one derivatives as well as seven-membered sultam analogues.

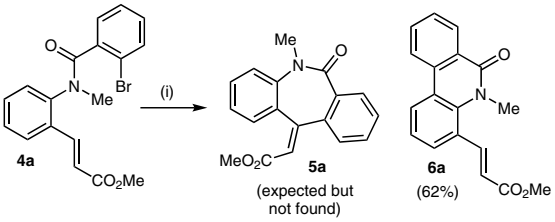
In our strategy, we used a common intermediate of type **4** as Heck precursors. Thus, bromo *N*-alkyl-substituted *N*-styrenyl benzamides **4a–k** and/or sulfonamides **4l**,**m** were prepared in 60–74% and 57–68% yields, respectively, via a chemoselective intermolecular Heck reaction[30] of disubstituted amides **3a–e** and/or sulfonamides **3f**,**g** with readily available acrylic acid derivatives. Intermediate precursors




**Scheme 2** Synthesis of bromo *N*-alkyl-substituted *N*-styrenyl benzamide/sulfonamide derivatives **4a–m**. *Reagents and conditions*: (i) $Et_3N$ (3.0 equiv), DCM, r.t., 6 h; (ii) NaH (1.5 equiv), DMF, r.t., 16 h; (iii) $Pd(OAc)_2$ (10 mol%), P(*o*-tol)$_3$ (20 mol%), $Et_3N$ (3.0 equiv), MeCN, 80 °C, 16 h; (iv) pyridine (5 mL), 60 °C, 12 h.

**3a–g** were in turn synthesized in 53–78% yields by two-step reactions of 2-iodoaniline (**1**) with commercially available 2-bromobenzoyl chloride or 2-bromobenzenesulfonyl chloride followed by N-alkylation of the resulting mono-substituted amide **2a**/sulfonamide **2b** (Scheme 2).[29,31]

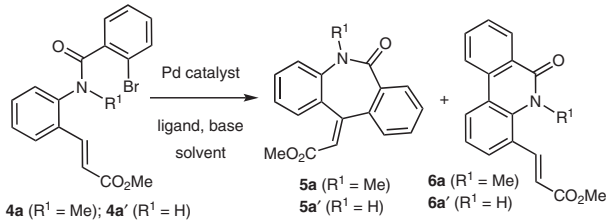
For the construction of dibenzoazepinone core, we initiated our investigation with the bromo *N*-alkyl-substituted *N*-styrenyl benzamide **4a** as a model precursor. Initially, when the substrate **4a** was reacted under the literature reported Heck conditions,[5] phenanthridinone framework **6a** was obtained as a major product (62%) instead of dibenzo[*b*,*e*]azepin-6-one derivative **5a** (Scheme 3). This could be easily explained by a more favorable 6-*exo*-trig process versus a 7-*exo*-trig mode of cyclization according to the Baldwin's rules.




**Scheme 3** Reaction of precursor **4a** under Heck conditions. *Reagents and conditions*: (i) $Pd(OAc)_2$ (25 mol%), $PPh_3$ (50 mol%), NaOAc (1.3 equiv), DMF, 100 °C, 8 h.

Therefore, in order to determine the optimum reaction conditions for the formation of our desired product **5a**, a series of experiments were carried out with the Heck precursor **4a**. The results are summarized in Table 1. When the reaction was performed with 5 mol% of $Pd(OAc)_2$ and 10 mol% of $PPh_3$ under heating in DMF at 110 °C for 10 hours in the

**Table 1** Optimization of Heck Conditions




| Entry | Catalyst (mol%) | Ligand (mol%) | Base (equiv) | Solvent | Temp ( °C) | Time (h) | Yield (%)[a] | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | **5** | **6** |
| 1[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | NaOAc (1.5) | DMF | 110 | 10 | **5a** (0) | **6a** (65) |
| 2[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | $Et_3N$ (1.5) | DMF | 110 | 10 | **5a** (0) | **6a** (57) |
| 3[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | DIPEA (1.5) | DMF | 110 | 10 | **5a** (15) | **6a** (27) |
| 4[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (1.5) | DMF | 110 | 5 | **5a** (63) | **6a** (0) |
| 5[b] | $Pd(OAc)_2$ (5) | $P(o\text{-tol})_3$ (10) | TMEDA (1.5) | DMF | 110 | 10 | **5a** (0) | **6a** (0) |
| 6[b,c] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | DMF | 110 | 5 | **5a** (75) | **6a** (0) |
| 7[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.5) | DMF | 110 | 5 | **5a** (75) | **6a** (0) |
| 8[b] | $Pd(OAc)_2$ (10) | $PPh_3$ (20) | TMEDA (2.0) | DMF | 110 | 5 | **5a** (75) | **6a** (0) |
| 9[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | DMF | 140 | 5 | **5a** (74) | **6a** (0) |
| 10[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | DMF | 80 | 16 | **5a** (46) | **6a** (0) |
| 11[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | MeCN | 80 | 16 | **5a** (30) | **6a** (0) |
| 12[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | DME | 110 | 8 | **5a** (41) | **6a** (0) |
| 13[b] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | THF | 80 | 10 | **5a** (23) | **6a** (0) |
| 14[b] | $Pd(PPh_3)_4$ (5) | $PPh_3$ (10) | TMEDA (2.0) | DMF | 110 | 10 | **5a** (5) | **6a** (48) |
| 15[b] | $Pd(PPh_3)_2Cl_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | DMF | 110 | 10 | **5a** (32) | **6a** (17) |
| 16[d,e] | $Pd(OAc)_2$ (5) | $PPh_3$ (10) | TMEDA (2.0) | DMF | 110 | 5 | **5a′** (0) | **6a′** (0) |

[a] Isolated yield.
[b] Reaction was carried out with precursor **4a** (0.27 mmol) in 5 mL of aforementioned solvent under sealed conditions.
[c] Optimized conditions.
[d] Reaction was carried out with precursor **4a′** (0.35 mmol) in 5 mL of DMF under sealed conditions.
[e] Debrominated product **4a′′** (Figure 2) was isolated in 45% yield.

presence of 1.5 equivalents of NaOAc and $Et_3N$, respectively, the phenanthridinone derivative **6a** was obtained in 65% and 57% yield, respectively, as the sole product (Table 1, entries 1 and 2). Interestingly, while conducting the reaction in the presence of DIPEA (diisopropylethylamine) as base under the same conditions, the desired product **5a** was obtained in 15% yield only along with 27% yield of unwanted compound **6a** (entry 3).

For further improvement of the yield of **5a** the reaction was repeated again with tetramethylethylenediamine (TMEDA) base, and to our delight, the reaction was completed in 5 hours and the product **5a** was isolated in 63% yield (Table 1, entry 4). Next, when substrate **4a** was subjected with 5 mol% of $Pd(OAc)_2$ and 10 mol% of P(*o*-tolyl)$_3$ in the presence of TMEDA in DMF under heating at 110 °C for 10 hours, the starting material **4a** was recovered unchanged (entry 5). The yield of dibenzoazepinone **5a** increased to 75% by increasing the amount of TMEDA (entry 6); however, additional 0.5 equivalent did not afford further improvement on the yield (entry 7). Increasing the amount of both the catalyst $Pd(OAc)_2$ and ligand $PPh_3$ did not improve the yield of product **5a** either (entry 8). When the reaction temperature was raised from 110 °C to 140 °C the yield of **5a** was found to be unaltered (entry 9). Decrease in temperature (80 °C) resulted in lower yield, though the reaction time was extended up to 16 hours (entry 10). The effect of other solvents on the yield of dibenzoazepinone **5a** was also investigated. It was observed that the use of either MeCN, dimethoxyethane (DME) or THF as solvents, however, were detrimental (entries 11–13). Other palladium catalysts such as $Pd(PPh_3)_4$ and $Pd(PPh_3)_2Cl_2$ were also used, but unfortunately a mixture of products **5a** and **6a** was obtained in both the cases (entries 14 and 15). From the above observations, we thus chose entry 6 as the optimized conditions for all of our future reactions. It is also to note that when the amide **4a′** was subjected to the optimized Heck conditions (entry 6), neither product **5a′** nor **6a′** was formed, instead the debrominated compound **4a″** was isolated in 45% yield (entry 16, Figure 2).

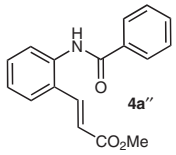
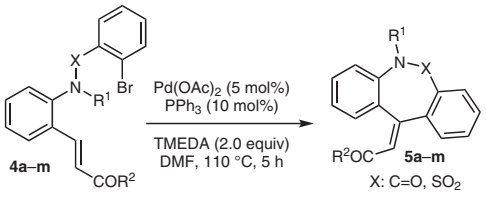



**Figure 2** Structure of the debrominated product **4a**″

The substrate scope of this methodology was investigated either using other acrylates or with different N-alkylated amides. Accordingly, substrates **4a–h** were treated under the optimized reaction conditions (Table 1, entry 6) to afford 6-oxo-5,6-dihydrodibenzo[*b*,*e*]azepin-11-ylidene acetic acid esters **5a–h** in 55–75% yields (Scheme 4). It was observed that the substrates having bulky groups like $CO_2t$-Bu and/or piperazine moiety in the acrylate motif **4f–h**, and **4k** resulted in relatively lower yields of the products **5f–h**, and **5k** compared to that of $CO_2Me$ group **5a–e**, probably owing to the steric factors. We then applied this methodology to the substrates **4i–k** containing acrylic acid amide moiety as electron-withdrawing group affording the corresponding dibenzoazepinone derivatives **5i–k**. Among these, compound **5k** is the *N*-methyl derivative of darenzepine. Furthermore, this optimized Heck protocol was successfully implemented to other types of precursors, bromo *N*-alkyl-substituted *N*-styrenyl sulfonamide derivatives **4l** and **4m** to afford biaryl fused seven-membered sultams **5l** and **5m**, respectively, in good yields (Scheme 4).




**5a**: X = CO, $R^1$ = Me, $R^2$ = OMe, 75%
**5b**: X = CO,$R^1$ = Et, $R^2$ = OMe, 71%
**5c**: X = CO, $R^1$ = $^n$Pr, $R^2$ = OMe, 70% (X-ray)
**5d**: X = CO, $R^1$ = $^i$Pr, $R^2$ = OMe, 73%
**5e**: X = CO, $R^1$ = $(CH_2)_2NMe_2$, $R^2$ = OMe, 68%
**5f**: X = CO, $R^1$ = $(CH_2)_2NMe_2$, $R^2$ = O$^t$Bu, 51%
**5g**: X = CO, $R^1$ = Me, $R^2$ = O$^t$Bu, 55%
**5h**: X = CO, $R^1$ = $^n$Pr, $R^2$ = O$^t$Bu, 57%
**5i**: X = CO, $R^1$ = Me, $R^2$ = $NMe_2$, 65%
**5j**: X = CO, $R^1$ = $^n$Pr, $R^2$ = $NMe_2$, 61%
**5k**: X = CO, $R^1$ = Me, $R^2$ = *N*-methylpiperazine, 53%
**5l**: X = $SO_2$, $R^1$ = Me, $R^2$ = O$^t$Bu, 57% (X-ray)
**5m**: X = $SO_2$, $R^1$ = $^n$Pr, $R^2$ = O$^t$Bu, 55%

**Scheme 4** Substrate scope of regioselective intramolecular Heck reaction. *Reagents and conditions*: **4** (100 mg), $Pd(OAc)_2$ (5 mol%), $PPh_3$ (10 mol%), TMEADA (2.0 equiv), DMF (2 mL), sealed tube, 110 °C, 5 h.

The structures of all the dibenzo[*b*,*e*]azepin-6-ones **5a–k** and sultam derivatives **5l**,**m** were established by their spectroscopic data. As representative examples, structures of **5c** and **5l** were also confirmed by single crystal X-ray diffraction study of which ORTEP diagrams are shown in Figure 3.[32] It is seen from the X-ray structures that the dibenzoazepinone and sultam derivatives possess *Z*- and *E*-configuration, respectively.

In our laboratory, we have also been engaged in identifying drug-like small molecular entities of medicinal importance.[33] Towards that goal and as an extension of this new methodology, we synthesized a novel compound **8** from dibenzoazepinone **5g** in a two-step reaction. Initially the ester hydrolysis of compound **5g** was performed using trifluoroacetic acid (TFA) to afford the corresponding acid derivative **7**, which was converted into the target amide **8** by amidation with *N*,*N*-dimethylethylenediamine under mild conditions (Scheme 5).

In conclusion, we have developed a new, convenient synthesis of dibenzo[*b*,*e*]azepin-6-ones and seven-mem-

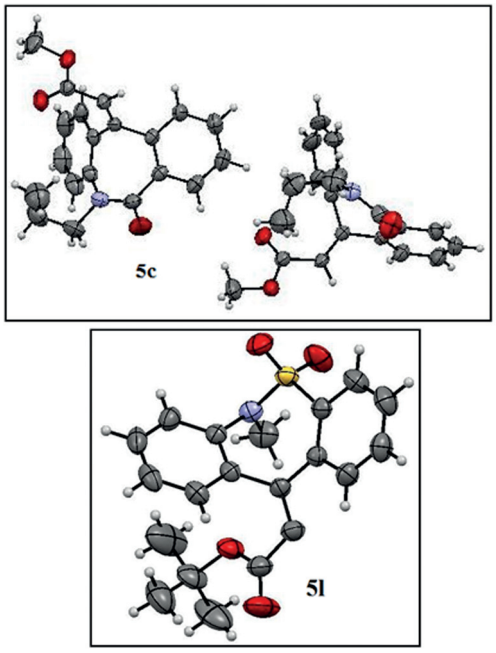
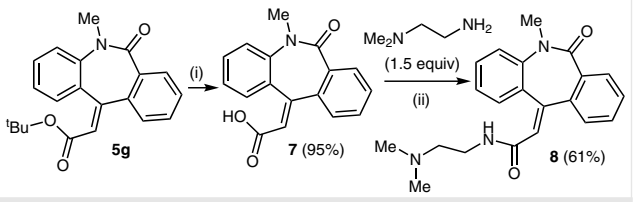



**Figure 3** X-ray crystal structures of compounds **5c** and **5l**




**Scheme 5** Hydrolysis followed by amidation of ester **5g**. *Reagents and conditions:* (i) TFA (1.5 equiv), DCM, r.t., 2 h; (ii) EDC·HCl (1.5 equiv), HOBt (1.5 equiv), DIPEA (3.0 equiv), THF, r.t., 16 h.

bered sultam derivatives in moderate to good yields (51–75%) via a Pd-catalyzed regioselective intramolecular Heck reaction of the corresponding easily accessible precursors, bromo *N*-alkyl-substituted *N*-styrenyl benzamide/sulfonamide derivatives. The protocol is simple and by employing this strategy we have achieved the *N*-methyl derivative of darenzepine in four steps in good yield. Further, we have synthesized a novel, non-cytotoxic (Supporting Information) small molecule **8** via implementation of this protocol. Preliminary docking studies were performed on compounds **5k** and **8** to understand their binding potential to muscarinic acetylcholine receptor subtype 4 (M4) (Supporting Information).

All chemicals and reagents used in current study were commercially available. Melting points were determined in open capillaries and are uncorrected. All the reactions were monitored by analytical TLC using 0.25 mm E-Merk precoated silica gel plates (60F254). Silica gel (100–200 mesh) was used for chromatographic separation. All the $^1$H NMR and $^{13}$C NMR spectra were recorded using a model DPX400 spectrometer (TOP Spin 2.1 Ultra shield$^{TM}$) in $CDCl_3$/DMSO-$d_6$ solvents and chemical shifts are reported in δ (ppm) units relative to the internal standard TMS. LCMS spectra were recorded on QTRAP Applied Biosystem/Shimadzu Autosampler, Agilent 6890 series with 5973 Mass selective detector. HRMS were recorded on XEVO G2-XS QTOF, and Waters QTOF Micro YA263 spectrometer, respectively. IR spectra were recorded on a PerkinElmer FTIR spectrophotometer by preparing a KBr pellet containing the title compound and are reported in wavelength numbers (cm$^{-1}$). Single crystal X-ray diffraction study was performed using Bruker Smart Apex-II diffractometer.

### 2-Bromo-*N*-(2-iodophenyl)benzamide (2a)[31]

To a stirred solution of 2-iodoaniline (**1**; 1.0 g, 4.56 mmol) in DCM (60 mL) was added $Et_3N$ (1.9 mL, 13.68 mmol) followed by 2-bromobenzoyl chloride (1.2 g, 5.47 mmol) at 0 °C under $N_2$ atmosphere and the reaction mixture was stirred at r.t. for 6 h. Then the mixture was diluted with DCM (40 mL). The combined organic layers were washed successively with sat. aq $NaHCO_3$ (2 × 25 mL), $H_2O$ (25 mL) and brine (25 mL), dried (anhyd $Na_2SO_4$), and concentrated. The crude material was purified by triturating with $Et_2O$/pentane to afford **2a** (1.4 g, 75%) as a white solid; mp 155–156 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 10.14 (s, 1 H, NH), 7.93 (d, *J* = 7.8 Hz, 1 H, ArH), 7.73 (d, *J* = 7.9 Hz, 1 H, ArH), 7.64 (d, *J* = 6.8 Hz, 1 H, ArH), 7.53 (t, *J* = 7.4 Hz, 1 H, ArH), 7.49–7.42 (m, 3 H, ArH), 7.0–7.05 (m, 1 H, ArH).

LCMS: *m*/*z* [M + H]$^+$ = 401.8.

### 2-Bromo-*N*-(2-iodophenyl)benzenesulfonamide (2b)[29]

To a stirred solution of 2-iodoaniline (**1**; 1.0 g, 4.56 mmol) in pyridine (5 mL) was added 2-bromobenzenesulfonyl chloride (1.4 g, 5.47 mmol) under $N_2$ atmosphere. Then the reaction mixture was heated at 60 °C for 12 h. Excess solvent was removed under reduced pressure and the crude mass was dissolved in DCM (100 mL). The organic layer was washed with $H_2O$ (3 × 25 mL) and brine (25 mL), dried (anhyd $Na_2SO_4$), and concentrated. The crude mass was purified by triturating with $Et_2O$/pentane to afford **2b** as a white solid (1.6 g, 82%); mp 105–107 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 9.93 (s, 1 H, NH), 7.88–7.84 (m, 3 H, ArH), 7.57–7.52 (m, 2 H, ArH), 7.29 (t, *J* = 7.6 Hz, 1 H, ArH), 7.01–6.96 (m, 2 H, ArH).

LCMS: *m*/*z* [M + H]$^+$ = 437.6.

### Disubstituted Amides 3a–e and Sulfonamides 3f,g;[31] 2-Bromo-*N*-(2-iodophenyl)-*N*-methylbenzamide 3a; Typical Procedure

To a stirred solution of 2-bromo-*N*-(2-iodophenyl)benzamide (**2a**; 1.4 g, 3.48 mmol) in DMF (10 mL) was added NaH (60% in oil, 209 mg, 5.22 mmol) portionwise at 0 °C under $N_2$ atmosphere and the stirring was continued for 30 min at 0 °C followed by dropwise addition of MeI (0.3 mL, 4.87 mmol). Then the reaction mixture was stirred at r.t. for 16 h and poured into ice-water (100 mL). The precipitate was collected by filtration and then washed with ice cold water and $Et_2O$/pentane, and dried in vacuo to afford **3a** (1.13 g, 78%) as an off-white solid; mp 123 °C.

Accordingly, other compounds **3b–e** were synthesized. However, the precursors **3f**,**g** were obtained following the above mentioned procedure starting from 2-bromo-*N*-(2-iodophenyl)benzenesulfonamide (**2b**) as starting material.

**Bromo *N*-Alkyl-Substituted *N*-Styrenyl Benzamides 4a–k and Sulfonamides 4l,m;[30] Methyl (*E*)-3-[2-(2-Bromo-*N*-methylbenzamido)phenyl]acrylate (4a); Typical Procedure**

To a degassed stirred mixture of 2-bromo-*N*-(2-iodophenyl)-*N*-methylbenzamide (**3a**; 500 mg, 1.20 mmol), methyl acrylate (0.1 mL, 1.20 mmol), $Et_3N$ (0.5 mL, 3.60 mmol) in anhyd MeCN (10 mL) was added P(*o*-tol)$_3$ (73 mg, 0.24 mmol) and $Pd(OAc)_2$ (27 mg, 0.12 mmol). Then the reaction mixture was heated at 80 °C for 16 h. The mixture was cooled to r.t. and diluted with $H_2O$ (20 mL). The organic parts were extracted with EtOAc (3 × 30 mL), and the combined organic extracts were washed with sat. aq $NaHCO_3$ (30 mL) and brine (30 mL), dried (anhyd $Na_2SO_4$), and concentrated under reduced pressure. The crude mass was purified by column chromatography (silica gel 100–200 mesh, 25–35% EtOAc/hexane) to afford **4a** (315.0 mg, 70%) as a brownish sticky solid.

IR (KBr): 3066, 2950, 2924, 2851, 1716, 1652, 1597, 1488 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 8.00 (d, *J* = 7.8 Hz, 1 H, ArH), 7.80 (d, *J* = 7.8 Hz, 1 H, ArH), 7.75 (d, *J* = 15.8 Hz, 1 H, C*H*=CHCO$_2$Me), 7.58 (t, *J* = 6.8 Hz, 1 H, ArH), 7.44 (d, *J* = 7.4 Hz, 1 H, ArH), 7.34 (t, *J* = 7.4 Hz, 1 H, ArH), 7.26 (t, *J* = 7.2 Hz, 1 H, ArH), 7.15–7.10 (m, 2 H, ArH), 6.65 (d, *J* = 15.9 Hz, 1 H, CH=C*H*CO$_2$Me), 3.77 (s, 3 H, OCH$_3$), 3.29 (s, 3 H, NCH$_3$).

LCMS: *m*/*z* [M + H]$^+$ = 374.0; [M + H + 2]$^+$ = 376.2.

Other compounds **4b–k** were synthesized accordingly. Similarly, sulfonamide derivatives **4l**,**m** were synthesized starting from the corresponding precursors **3f**,**g**.

**Dibenzo[*b*,*e*]azepin-6-ones 5a–k and Sultam Derivatives 5l,m; Methyl (*Z*)-2-(5-Methyl-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetate (5a); Typical Procedure**

To a degassed stirred mixture of methyl (*E*)-3-[2-(2-bromo-*N*-methylbenzamido)phenyl]acrylate (**4a**; 100 mg, 0.27 mmol) and TMEDA (8 µL, 0.54 mmol) in anhyd DMF (2 mL) was added $PPh_3$ (7 mg, 0.027 mmol) and $Pd(OAc)_2$ (3 mg, 0.01 mmol). Then the reaction mixture was heated at 110 °C for 5 h in a sealed tube. The mixture was cooled to r.t. and diluted with ice cold $H_2O$ (10 mL). The organic phase was extracted with EtOAc (3 × 30 mL), and the combined organic layers were washed with $H_2O$ (3 × 20 mL) and brine (15 mL), and dried (anhyd $Na_2SO_4$). The solvent was evaporated under reduced pressure and the crude mass obtained was purified by column chromatography (silica gel 100–200 mesh) eluting with 40–45% EtOAc/hexane to afford **5a** (59 mg, 75%) as a white solid; mp 131–132 °C.

IR (KBr): 2950, 2924, 2852, 1726, 1637 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 7.4 Hz, 1 H, ArH), 7.46 (t, *J* = 7.2 Hz, 1 H, ArH), 7.40 (t, *J* = 7.2 Hz, 1 H, ArH), 7.33–7.27 (m, 2 H, ArH), 7.23 (d, *J* = 7.4 Hz, 2 H, ArH), 7.14 (t, *J* = 7.2 Hz, 1 H, ArH), 6.15 (s, 1 H, C=C*H*CO$_2$Me), 3.66 (s, 3 H, OCH$_3$), 3.58 (s, 3 H, NCH$_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.3, 165.3, 154.3, 142.8, 138.9, 135.2, 131.9, 131.2, 130.93, 128.9, 128.9, 128.3, 125.2, 124.8, 122.6, 119.5, 51.5, 37.8.

LCMS: *m*/*z* [M + H]$^+$ = 294.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_3Na$: 316.0950; found: 316.0940.

**Methyl (*Z*)-3-(2-Benzamidophenyl)acrylate (4a″) (Table 1, entry 16)**

The product was obtained by reacting the N-unsubstituted amide **4a′** following the typical procedure and isolated by column chromatography (eluent: hexanes/EtOAc 2:1) as a colorless sticky solid (35 mg, 45%).

IR (KBr): 3353, 3042, 2939, 2845, 1720, 1651 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 10.31 (s, 1 H, NH), 8.00 (d, *J* = 7.2 Hz, 2 H, ArH), 7.90 (d, *J* = 7.3 Hz, 1 H, ArH), 7.75 (d, *J* = 15.9 Hz, 1 H, C*H*=CHCO$_2$Me), 7.62 (d, *J* = 7.2 Hz, 1 H, ArH), 7.58–7.54 (m, 2 H, ArH), 7.50–7.46 (m, 1 H, ArH), 7.39 (d, *J* = 7.6 Hz, 1 H, ArH), 7.34 (t, *J* = 7.6 Hz, 1 H, ArH), 6.62 (d, *J* = 15.9 Hz, 1 H, CH=C*H*CO$_2$Me), 3.72 (s, 3 H, OCH$_3$).

LCMS: *m*/*z* [M + H]$^+$ = 282.1.

**Methyl (*Z*)-2-(5-Ethyl-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetate (5b)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:1) as a colorless sticky solid (56 mg, 71%).

IR (KBr): 2955, 2927, 2867, 1728, 1634 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 7.72 (d, *J* = 7.4 Hz, 1 H, ArH), 7.55–7.50 (m, 2 H, ArH), 7.45 (t, *J* = 7.4 Hz, 1 H, ArH), 7.38–7.31 (m, 2 H, ArH), 7.19 (d, *J* = 3.8 Hz, 2 H, ArH), 6.28 (s, 1 H, C=C*H*CO$_2$Me), 4.49 (q, *J* = 6.9 Hz, 1 H, NC*H*$_a$H$_b$CH$_3$), 3.69 (q, *J* = 6.9 Hz, 1 H, NCH$_a$*H*$_b$CH$_3$), 1.06 (t, *J* = 6.9 Hz, 3 H, NCH$_2$C*H*$_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 166.9, 165.4, 154.1, 143.0, 137.9, 137.2, 131.7, 131.6, 130.9, 128.9, 128.8, 127.9, 125.6, 124.4, 123.9, 119.3, 51.4, 44.6, 13.3.

LCMS: *m*/*z* [M + H]$^+$ = 308.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}NO_3$: 308.1287; found: 308.1282.

**Methyl (*Z*)-2-(6-Oxo-5-propyl-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetate (5c)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:1) as a white solid (56 mg, 70%); mp 117–118 °C.

IR (KBr): 2957, 2926, 2871, 1727, 1634 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 7.2 Hz, 1 H, ArH), 7.44–7.36 (m, 2 H, ArH), 7.29–7.28 (m, 2 H, ArH), 7.20 (d, *J* = 7.0 Hz, 2 H, ArH), 7.14 (t, *J* = 7.0 Hz, 1 H, ArH), 6.16 (s, 1 H, C=C*H*CO$_2$Me), 4.67–4.59 (m, 1 H, NC*H*$_a$H$_b$CH$_2$CH$_3$), 3.64 (s, 3 H, OCH$_3$), 3.62–3.57 (m, 1 H, NCH$_a$*H*$_b$CH$_2$CH$_3$), 1.67–1.62 (m, 1 H, NCH$_2$C*H*$_a$H$_b$CH$_3$), 1.59–1.52 (m, 1 H, NCH$_2$CH$_a$*H*$_b$CH$_3$), 0.84 (t, *J* = 7.2 Hz, 3 H, NCH$_2$CH$_2$C*H*$_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.1, 165.3, 154.4, 143.0, 137.7, 137.3, 131.7, 131.6, 131.0, 128.9, 128.7, 128.1, 125.5, 124.5, 123.9, 119.2, 51.4, 50.8, 21.0, 11.1.

LCMS: *m*/*z* [M + H]$^+$ = 321.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}NO_3$: 322.1443; found: 322.1445.

**Methyl (*Z*)-2-(5-Isopropyl-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetate (5d)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:1) as a white solid (58 mg, 73%); mp 125–127 °C.

IR (KBr): 2959, 2925, 2874, 1725, 1632 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 7.71 (d, $J$ = 7.2 Hz, 1 H, ArH), 7.50 (td, $J$ = 7.4, 0.8 Hz, 1 H, ArH), 7.45–7.42 (m, 2 H, ArH), 7.34–7.29 (m, 2 H, ArH), 7.23–7.17 (m, 2 H, ArH), 6.29 (s, 1 H, C=C*H*$CO_2$Me), 4.63–4.56 (m, 1 H, NC*H*$Me_2$), 3.59 (s, 3 H, $OCH_3$), 1.51 [d, $J$ = 6.8 Hz, 3 H, NCH($CH_3$)$_a$($CH_3$)$_b$], 1.15 [d, $J$ = 6.8 Hz, 3 H, NCH($CH_3$)$_a$($CH_3$)$_b$].

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.5, 165.4, 154.5, 143.2, 139.5, 135.9, 132.2, 131.3, 131.0, 128.9, 128.0, 127.7, 126.2, 125.3, 124.3, 118.8, 52.2, 51.4, 22.8, 20.6.

LCMS: $m/z$ [M + H]$^+$ = 322.4.

HRMS (ESI): $m/z$ [M + H]$^+$ calcd for $C_{20}H_{20}NO_3$: 322.1443; found: 322.1436.

**Methyl (*Z*)-2-{5-[2-(Dimethylamino)ethyl]-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene}acetate (5e)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:4) as a brown sticky solid (55 mg, 68%).

IR (KBr): 2957, 2922, 2857, 1727, 1631 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, $J$ = 6.7 Hz, 1 H, ArH), 7.43–7.36 (m, 3 H, ArH), 7.31–7.29 (m, 1 H, ArH), 7.21–7.14 (m, 3 H, ArH), 6.15 (s, 1 H, C=C*H*$CO_2$Me), 4.75–4.72 (m, 1 H, NC$H_a$$H_b$$CH_2$$NMe_2$), 3.77–3.73 (m, 1 H, NC$H_a$$H_b$$CH_2$$NMe_2$), 3.65 (s, 3 H, $OCH_3$), 2.51 (t, $J$ = 7.0 Hz, 2 H, $NCH_2$C$H_2$$NMe_2$), 2.20 [s, 6 H, N($CH_3$)$_2$].

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 166.7, 163.7, 151.9, 142.6, 137.5, 136.8, 131.3, 130.7, 130.4, 128.4, 128.3, 127.7, 125.3, 124.1, 123.2, 121.4, 55.6, 51.4, 46.7, 44.4.

LCMS: $m/z$ [M + H]$^+$ = 350.9.

HRMS (ESI): $m/z$ [M + H]$^+$ calcd for $C_{21}H_{23}N_2O_3$: 351.1709; found: 351.1711.

***tert*-Butyl (*Z*)-2-{5-[2-(Dimethylamino)ethyl]-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene}acetate (5f)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:4) as a brown sticky solid (42 mg, 51%).

IR (KBr): 3050, 2962, 2927, 2872, 1706, 1633 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, $J$ = 7.2 Hz, 1 H, ArH), 7.43–7.27 (m, 4 H, ArH), 7.20–7.14 (m, 3 H, ArH), 6.05 (s, 1 H, C=C*H*$CO_2$*t*-Bu), 4.80–4.73 (m, 1 H, NC$H_a$$H_b$$CH_2$$NMe_2$), 3.92–3.85 (m, 1 H, NC$H_a$$H_b$$CH_2$$NMe_2$), 2.70 (s, 2 H, $NCH_2$C$H_2$$NMe_2$), 2.34 [s, 6 H, N($CH_3$)$_2$], 1.32 [s, 9 H, C($CH_3$)$_3$].

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 166.9, 164.0, 151.2, 142.6, 137.4, 136.8, 131.3, 130.7, 130.4, 128.4, 128.3, 127.7, 125.3, 124.1, 123.2, 121.6, 80.6, 55.9, 46.7, 44.4, 27.4.

LCMS: $m/z$ [M + H]$^+$ = 393.2.

HRMS (ESI): $m/z$ [M + H]$^+$ calcd for $C_{24}H_{29}N_2O_3$: 393.2178; found: 393.2172.

***tert*-Butyl (*Z*)-2-(5-Methyl-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetate (5g)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:1) as a white solid (44 mg, 55%); mp 123–127 °C.

IR (KBr): 3035, 2961, 2924, 2875, 1708, 1637 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, $J$ = 7.4 Hz, 1 H, ArH), 7.45 (t, $J$ = 7.4 Hz, 1 H, ArH), 7.38 (t, $J$ = 7.4 Hz, 1 H, ArH), 7.29–7.25 (m, 3 H, ArH), 7.17–7.13 (m, 2 H, ArH), 6.06 (s, 1 H, C=C*H*$CO_2$*t*-Bu), 3.58 (s, 3 H, $NCH_3$), 1.29 [s, 9 H, C($CH_3$)$_3$].

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.5, 164.6, 151.5, 142.9, 138.9, 136.2, 131.8, 131.1, 130.9, 128.6, 128.5, 128.1, 125.2, 124.7, 122.5, 122.4, 80.8, 37.7, 27.7.

LCMS: $m/z$ [M + H]$^+$ = 336.2.

HRMS (ESI): $m/z$ [M + H]$^+$ calcd for $C_{21}H_{22}NO_3$: 336.1600; found: 336.1604.

***tert*-Butyl (*Z*)-2-(6-Oxo-5-propyl-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetate (5h)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:1) as a white solid (46 mg, 57%); mp 111–112 °C.

IR (KBr): 2963, 2926, 2873, 1704, 1638 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, $J$ = 7.4 Hz, 1 H, ArH), 7.41 (t, $J$ = 7.2 Hz, 1 H, ArH), 7.36 (t, $J$ = 7.2 Hz, 1 H, ArH), 7.29 (t, $J$ = 8.0 Hz, 2 H, ArH), 7.20 (d, $J$ = 8.0 Hz, 2 H, ArH), 7.13 (t, $J$ = 7.4 Hz, 1 H, ArH), 6.06 (s, 1 H, C=C*H*$CO_2$*t*-Bu), 4.70–4.63 (m, 1 H, NC$H_a$$H_b$$CH_2$$CH_3$), 3.63–3.56 (m, 1 H, NC$H_a$$H_b$$CH_2$$CH_3$), 1.69–1.54 (m, 2 H, $NCH_2$C$H_2$$CH_3$), 1.31 [s, 9 H, C($CH_3$)$_3$], 0.86 (t, $J$ = 7.4 Hz, 3 H, $NCH_2CH_2$C$H_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.3, 164.5, 152.0, 143.2, 138.2, 137.3, 131.6, 131.6, 131.0, 128.7, 128.5, 128.4, 125.4, 124.6, 123.8, 121.9, 80.9, 50.7, 27.8, 21.0, 11.2.

LCMS: $m/z$ [M + H]$^+$ = 364.1.

HRMS (ESI): $m/z$ [M + H]$^+$ calcd for $C_{23}H_{26}NO_3$: 364.1913; found: 364.1920.

**(*Z*)-*N*,*N*-Dimethyl-2-(5-methyl-6-oxo-5*H*- dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetamide (5i)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 2:3) as a white solid (51 mg, 65%); mp 173–174 °C.

IR (KBr): 3066, 2921, 1632, 1614 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 7.78 (d, $J$ = 7.6 Hz, 1 H, ArH), 7.56 (t, $J$ = 7.4 Hz, 1 H, ArH), 7.46–7.43 (m, 2 H, ArH), 7.37–7.34 (m, 2 H, ArH), 7.16 (t, $J$ = 7.4 Hz, 1 H, ArH), 7.10 (d, $J$ = 7.6 Hz, ArH), 6.48 (s, 1 H, C=C*H*$CONMe_2$), 3.46 (s, 3 H, $NCH_3$), 2.88 [s, 3 H, N($CH_3$)$_a$($CH_3$)$_b$], 2.73 [s, 3 H, N($CH_3$)$_a$($CH_3$)$_b$].

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.5, 166.6, 143.3, 142.3, 139.1, 135.1, 131.7, 130.8, 130.6, 128.5, 128.1, 127.8, 125.4, 125.3, 123.1, 122.0, 37.7, 37.0, 34.1.

LCMS: $m/z$ [M + H]$^+$ = 307.2.

HRMS (ESI): $m/z$ [M + H]$^+$ calcd for $C_{19}H_{19}N_2O_2$: 307.1447; found: 307.1442 and $m/z$ [M + K]$^+$ calcd for $C_{19}H_{18}N_2O_2K$: 345.1005; found: 345.1006.

**(*Z*)-*N*,*N*-Dimethyl-2-(6-oxo-5-propyl-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetamide (5j)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 2:3) as a white solid (49 mg, 61%); mp 137–140 °C.

IR (KBr): 3029, 2964, 2920, 2850, 1636, 1607 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, $J$ = 7.3 Hz, 1 H, ArH), 7.43 (t, $J$ = 7.2 Hz, 1 H, ArH), 7.37 (t, $J$ = 7.2 Hz, 1 H, ArH), 7.32–7.28 (m, 3 H, ArH), 7.12 (t, $J$ = 7.3 Hz, 1 H, ArH), 6.32 (s, 1 H, C=C*H*$CONMe_2$), 4.22–4.14 (m, 1 H, NC$H_a$$H_b$$CH_2$$CH_3$), 3.83–3.76 (m, 1 H, NC$H_a$$H_b$$CH_2$$CH_3$), 2.94 [s, 3 H, N($CH_3$)$_a$($CH_3$)$_b$], 2.88 [s, 3 H, N($CH_3$)$_a$($CH_3$)$_b$], 1.89–1.84 (m, 1 H, $NCH_2$C$H_a$$H_b$$CH_3$), 1.80–1.69 (m, 1 H, $NCH_2CH_a$$H_b$$CH_3$), 0.94 (t, $J$ = 7.4 Hz, 3 H, $NCH_2CH_2$C$H_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.6, 166.4, 145.3, 143.0, 138.6, 136.6, 131.9, 131.6, 130.9, 128.7, 128.5, 128.4, 125.6, 125.4, 122.9, 52.5, 37.7, 34.6, 21.6, 11.5.

LCMS: *m*/*z* [M + H]$^+$ = 335.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{23}N_2O_2$: 335.1760; found: 335.1447 and *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{22}N_2O_2Na$: 357.1579; found: 357.1723.

**(*Z*)-5-Methyl-11-[2-(4-methylpiperazin-1-yl)-2-oxoethylidene]-5*H*-dibenzo[*b*,*e*]azepin-6(11*H*)-one (5k)**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:3) as a white solid (43 mg, 53%); mp 165–168 °C.

IR (KBr): 3063, 2981, 2925, 1631, 1615 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 7.79 (d, *J* = 7.6 Hz, 1 H, ArH), 7.57 (t, *J* = 7.4 Hz, 1 H, ArH), 7.47–7.43 (m, 2 H, ArH), 7.41–7.34 (m, 2 H, ArH), 7.19 (t, *J* = 7.4 Hz, 1 H, ArH), 7.11 (d, *J* = 7.6 Hz, 1 H, ArH), 6.41 (s, 1 H, C=CHCON), 3.46 (s, 3 H, $NCH_3$), 3.25–3.23 (m, 1 $H_{piperazine}$), 2.54 (s, 3 H, piperazine $NCH_3$), 2.27–2.23 (m, 2 $H_{piperazine}$), 2.04 (s, 3 $H_{piperazine}$), 1.86–1.83 (m, 1 $H_{piperazine}$), 1.46–1.44 (m, 1 $H_{piperazine}$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 168.0, 165.7, 143.2, 142.4, 139.6, 135.2, 132.2, 131.2, 130.9, 129.1, 128.6, 128.3, 126.0, 125.8, 123.0, 122.5, 54.9, 54.1, 46.0, 45.8, 41.0, 38.1.

LCMS: *m*/*z* [M + H]$^+$ = 362.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}N_3O_2$: 362.1869; found: 362.1861.

**Sultam Derivative 5l**

The product was isolated by column chromatography (eluent: hexanes/EtOAc 1:3) as a white solid (47 mg, 57%); mp 166–168 °C.

IR (KBr): 3078, 2981, 2875, 1710, 1333, 1156 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 7.83 (d, *J* = 7.4 Hz, 1 H, ArH), 7.69–7.61 (m, 3 H, ArH), 7.54–7.48 (m, 2 H, ArH), 7.43 (t, *J* = 7.0 Hz, 1 H, ArH), 7.25 (d, *J* = 7.4 Hz, 1 H, ArH), 6.49 (s, 1 H, C=C*H*$CO_2$*t*-Bu), 3.47 (s, 3 H, $NCH_3$), 1.16 [s, 9 H, $C(CH_3)_3$].

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 164.6, 149.6, 140.5, 140.0, 136.0, 135.7, 132.2, 130.2, 130.0, 129.9, 129.2, 128.9, 128.6, 128.2, 127.5, 81.6, 38.6, 27.6.

LCMS: *m*/*z* [M + Na]$^+$ = 394.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{21}NO_4SNa$: 394.1089; found: 394.1088.

**Sultam Derivative 5m**

The product was isolated by column chromatography (eluent: hexanes/EtOAc, 1:3) as a white solid (46 mg, 55%); mp 147–149 °C.

IR (KBr): 2986, 2958, 2876, 1710, 1331, 1142 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 7.82 (d, *J* = 7.0 Hz, 1 H, ArH), 7.68–7.60 (m, 3 H, ArH), 7.51–7.42 (m, 3 H, ArH), 7.28 (d, *J* = 7.0 Hz, 1 H, ArH), 6.48 (s, 1 H, C=C*H*$CO_2$*t*-Bu), 3.72 (br s, 1 H, $NCH_aH_bCH_2CH_3$), 3.51 (br s, 1 H, $NCH_aH_bCH_2CH_3$), 1.61–1.56 (m, 2 H, $NCH_2CH_2CH_3$), 1.16 [s, 9 H, $C(CH_3)_3$], 0.92 (t, *J* = 7.3 Hz, 3 H, $NCH_2CH_2CH_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 164.5, 149.9, 140.8, 140.5, 135.9, 134.5, 132.0, 131.4, 130.1, 129.7, 129.4, 128.8, 128.7, 128.3, 127.2, 81.5, 53.0, 27.7, 22.7, 10.9.

LCMS: *m*/*z* [M + H]$^+$ = 400.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{26}NO_4S$: 400.1583; found: 400.1587.

**Methyl (*E*)-3-(5-Methyl-6-oxo-5,6-dihydrophenanthridin-4-yl)acrylate (6a) (Scheme 3)**

This compound was prepared by following the literature reported Heck conditions[5] and was isolated by column chromatography (eluent: hexanes/EtOAc 3:2) as a white solid (62%); mp 102–105 °C.

IR (KBr): 3036, 2975, 2924, 2851, 1717, 1639 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 8.54 (d, *J* = 8.0 Hz, 2 H, ArH), 8.34 (d, *J* = 8.0 Hz, 1 H, ArH), 8.14 (d, *J* = 15.9 Hz, 1 H, C*H*=CHCO$_2$Me), 7.87 (t, *J* = 7.4 Hz, 1 H, ArH), 7.74 (d, *J* = 7.3 Hz, 1 H, ArH), 7.67 (t, *J* = 7.4 Hz, 1 H, ArH), 7.39 (t, *J* = 7.7 Hz, 1 H, ArH), 6.47 (d, *J* = 15.8 Hz, 1 H, CH=C*H*$CO_2$Me), 3.76 (s, 3 H, $OCH_3$), 3.64 (s, 3 H, $NCH_3$).

LCMS: *m*/*z* [M + H]$^+$ = 294. 0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}NO_3$: 294.1130; found: 294.1119 and *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_3Na$: 316.0950; found: 316.0936.

**2-(5-Methyl-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetic Acid (7)**

To a stirred solution of compound **5g** (250.0 mg, 0.75 mmol) in DCM (10 mL) was added TFA (8.0 µL, 1.12 mmol) at 0 °C under $N_2$ atmosphere and the reaction mixture was stirred at r.t. for 2 h. Then the mixture was concentrated under reduced pressure and the crude material was purified by triturating with $Et_2O$/pentane to afford **7** (198.0 mg, 95%) as white solid; mp 195 °C.

IR (KBr): 3405, 2930, 2851, 1719, 1633 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 12.52 (s, 1 H, $CO_2H$), 7.77 (d, *J* = 7.4 Hz, 1 H, ArH), 7.54 (t, *J* = 7.0 Hz, 1 H, ArH), 7.48–7.43 (m, 2 H, ArH), 7.35–7.33 (m, 2 H, ArH), 7.23–7.17 (m, 2 H, ArH), 6.18 (s, 1 H, C=C*H*-$CO_2H$), 3.47 (s, 3 H, $NCH_3$).

LCMS: *m*/*z* [M + H]$^+$ = 280.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}NO_3$: 280.0974; found: 280.0975.

***N*-[2-(Dimethylamino)ethyl]-2-(5-methyl-6-oxo-5*H*-dibenzo[*b*,*e*]azepin-11(6*H*)-ylidene)acetamide (8)**

To a stirred solution of **7** (150.0 mg, 0.54 mmol) in THF (10 mL) were added EDC·HCl (154.5 mg, 0.81 mmol), HOBt (108.8 mg, 0.81 mmol) and DIPEA (0.3 mL, 1.62 mmol). The reaction mixture was stirred for 10 min under ice cooling and *N*,*N*-dimethylethylenediamine (8 µL, 0.81 mmol) was added to the mixture. The mixture and stirred at r.t. for 16 h and diluted with ice-water (10 mL). The organic phase was extracted with EtOAc (2 × 25 mL) and the combined organic layers were washed successively with water (2 × 15 mL) followed by brine (20 mL) and dried (anhyd $Na_2SO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 100–200 mesh, 60% EtOAc in hexane) to afford **8** (124.0 mg, 61%) as an off-white solid; mp 136–138 °C.

IR (KBr): 2981, 2925, 2873, 1636, 1615 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 7.95 (br s, 1 H, NH), 7.75 (d, *J* = 7.2 Hz, 1 H, ArH), 7.55 (t, *J* = 7.2 Hz, 1 H, ArH), 7.45–7.40 (m, 2 H, ArH), 7.32–7.30 (m, 2 H, ArH), 7.19–7.11 (m, 2 H, ArH), 6.29 (s, 1 H, C=C*H*-CONH), 3.46 (s, 3 H, $NCH_3$), 3.15–3.12 (m, 2 H, $NHCH_2CH_2NMe_2$), 2.25–2.20 (m, 2 H, $NHCH_2CH_2NMe_2$), 2.10 [s, 6 H, $(NCH_3)_2$].

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.7, 165.4, 146.7, 142.9, 139.5, 135.2, 132.0, 131.1, 130.9, 128.9, 128.5, 128.3, 125.7, 125.0, 124.9, 122.6, 56.8, 44.7, 37.6, 36.2.

LCMS: *m*/*z* [M + H]$^+$ = 350.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{24}N_3O_2$: 350.1869; found: 350.1855 and *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{23}N_3O_2Na$: 372.1688; found: 372.1673.

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## Notes

The authors declare no competing financial interest.

## Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611548.

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