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Note

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Synthesis of 2,3-Dihydro-1*H*-2-benzazepin-1-ones and 3*H*-2-Benzoxepin-1-ones by Isocyanide-based Multicomponent Reaction/Wittig Sequence Starting from Phosphonium Salt Precursors

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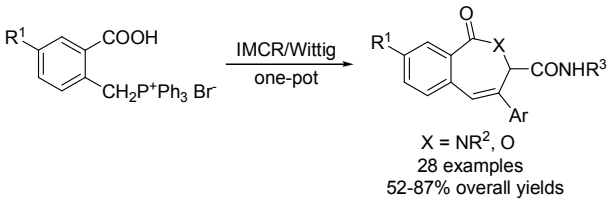


ABSTRACT: A one-pot synthesis of multisubstituted 2,3-dihydro-1*H*-2-benzazepin-1-ones and 3*H*-2-benzoxepin-1-ones by an I-MCR/Wittig Sequence was developed. The reaction of phosphonium salt **3**, arylglyoxals **4**, amine **5** (or without), and isocyanide **6** produced the 2,3-dihydro-1*H*-2-benzazepin-1-ones **8** or 3*H*-2-benzoxepin-1-ones **10** in good yields via a sequential Ugi or Passerini condensation and intramolecular Wittig reaction in the presence of NEt_3.

Key words: 1*H*-2-benzazepin-1-one; 3*H*-2-benzoxepin-1-one; Ugi reaction; Passerini reaction; intramolecular Wittig reaction; isocyanide

Multicomponent reactions (MCRs) have become an essential tool in organic and medicinal chemistry because they are one-pot processes bringing together three or more components and show

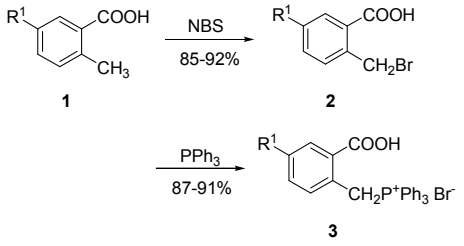
high efficiency for rapid access to natural product and druglike small molecules with diverse molecular structures. The isocyanide based multicomponent reactions (I-MCRs), mainly Ugi and Passerini reaction, are extremely useful tools for synthesis of combinatorial libraries of compounds.[1] The sequences of Ugi and Passerini reactions, followed by post-condensation transformations, constitute extremely powerful synthetic tools for the preparation of structurally diverse complex molecules, among them are heterocyclic compounds with elaborate substitution patterns.[2] For example, some sequential I-MCRs and Diels-Alder, Pictet-Spengler, Heck, Smiles-Metathesis, S_N2 reaction have been utilized in preparation of various heterocycles.[3]

The Wittig reaction of phosphorus ylide with carbonyl compound provides a powerful method for construction of C=C double bond via inter- or intramolecular fashion under mild reaction condition.[4] Intramolecular Wittig reaction has become a useful tool in preparation of various five, six, seven and large membered heterocycles through intramolecular cyclization.[5] Thus, it is envisioned that combining the efficiency of the I-MCRs with a post-condensation Wittig reaction would facilitate access to a series of biologically useful heterocycles. Indeed, the sequence of I-MCRs/Horner reaction has been used in preparation of butenolides, pyrrolidinones and pyridones.[6] However, the sequence of I-MCRs starting from phosphonium salt precursors, followed by postcondensation of intramolecular Wittig reaction, was not previously reported.

The synthesis of 2-benzazepines has been the focus of continuing interest because these ring systems lie at the heart of a great number of poly- and diversely functionalized compounds, that have shown broad spectrum of biological properties. For example, some of the 2-benzazepines have been found to be potent analgesic or anticonvulsant agents,[7] phenylethanolamine N-methyltransferase inhibitors,[8] 2,4-diaminopyrimidine c-Met inhibitors,[9] melanin-concentrating hormone receptor 1 antagonists,[10] and

N-methyl-D-aspartate receptor antagonists.[11] The range of biological activities and characteristic chemical structures have made synthetic studies of 2-benzazepines very attractive.[12] However, the corresponding 2,3-dihydro-1*H*-2-benzazepin-1-ones and 3*H*-2-benzoxepin-1-ones were seldom reported in the literature. Recently we have been interested in the synthesis of various heterocycles via aza-Wittig or multicomponent reactions.[13] Herein we wish to report a new efficient synthesis of multisubstituted 2,3-dihydro-1*H*-2-benzazepin-1-ones and 3*H*-2-benzoxepin-1-ones by an I-MCR/Wittig sequence starting from phosphonium salt precursors.

The phosphonium salt precursors **3** (Scheme 1) were synthesized according to standard protocols.[14] Bromination of 2-methyl-benzoic acid derivatives **1** with the NBS led to 2-bromomethyl-benzoic acid derivatives **2**, which were converted to the corresponding phosphonium salts **3** via reaction with triphenylphosphine.

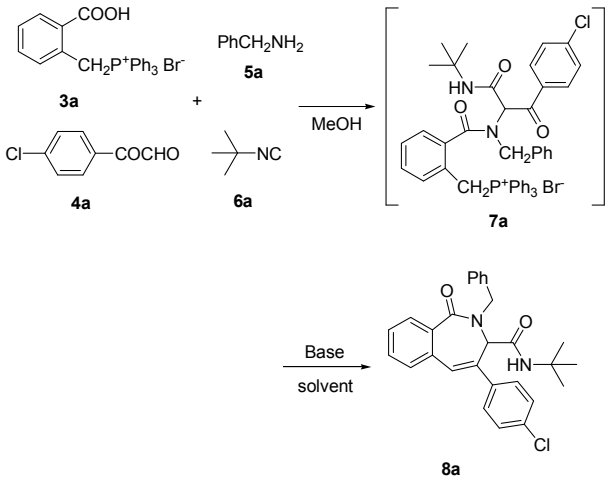


1 **2** **3**

Scheme 1. Preparation of phosphonium salt precursors **3**

Initially, we selected the phosphonium salt **3a**, 4-chlorophenylglyoxal **4a**, benzylamine **5a** and *t*-butylisocyanide **6a** as the reactants (Scheme 2). When the phosphonium salt **3a**, 4-chlorophenylglyoxal **4a**, benzylamine **5a** and *t*-butylisocyanide **6a** was stirred in methanol at room temperature for 24 h, the Ugi product **7a** was often obtained as semi-solid or oil which was difficult to be purified. So after washed by ether/petroleum ether (V/V = 1:1), the crude phosphonium salt **7a** was used directly without further purification for intramolecular Wittig reaction. The solvent and base used had remarkable effect on this reaction. In case that the solid K_2CO_3 was used as base at 60 °C,

moderate to good yields of the product **8a** were obtained when THF or toluene were utilized as solvents (52-71%, Table 1, entry 1-2). However, no product was got as K_2CO_3/MeOH was utilized (Table 1, entry 3), probably due to decomposition of the intermediate **7a** under the more polar solvent condition. Relatively lower yields were obtained when K_2CO_3/toluene system was used at room or refluxing temperature (45-56%, Table 1, entry 4-5). Utilizing the more basic NaOH also resulted in lower yield of the product (35%, Table 1, entry 6). The best result was obtained (87%, Table 1, entry 7-9) when NEt_3 was used as base at toluene refluxing temperature.



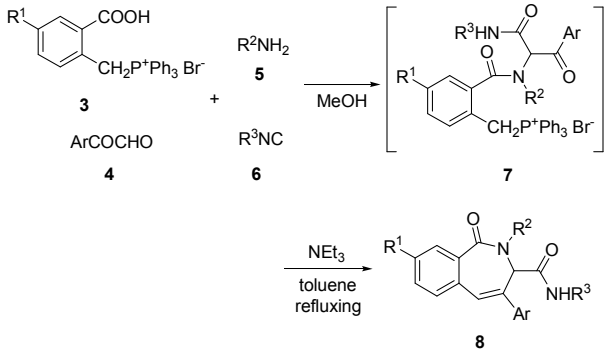
Scheme 2. Optimization of the reaction condition

Table 1. Screening reactions conditions for intramolecular Wittig reaction

entry	solvent	Condition	base	Yield[a] (%)
1	THF	60 °C /2 h	K_2CO_3	52
2	toluene	60 °C/2 h	K_2CO_3	71
3	MeOH	60 °C /2 h	K_2CO_3	0
4	toluene	rt/24 h	K_2CO_3	56
5	toluene	reflux/1 h	K_2CO_3	45
6	toluene	60°C/1 h	NaOH	35
7	toluene	60°C/12 h	NEt_3	61
8	toluene	reflux/2 h	NEt_3	87
9	MeOH	reflux/12 h	NEt_3	72

[a] Isolated yields.

With the optimized condition, various phosphonium salt **3**, arylglyoxals **4**, amine **5** and isocyanide **6** were employed for the reaction (Scheme 3). All of the reactions were carried out smoothly to give the corresponding 2,3-dihydro-1*H*-2-benzazepin-1-ones **8** in toluene at reflux temperature, and moderate to satisfactory yields were obtained with various substituents on the reactants (Table 2). Various amines can be used in above one-pot cyclization to prepare 2,3-dihydro-1*H*-2-benzazepin-1-ones **8**. As aromatic amine substituted by ester group (compounds **8s** and **8t**, R^2 = 2-$MeOOCC_6H_4$) was used, moderate yields (51-55%) of the products were obtained, however, no products were reached when other amines with strong electron-withdrawing group (R^2 = 4-$MeCOC_6H_4$, 4-NCC_6H_4 and 4-$NO_2C_6H_4$) were utilized. Better yields (62-87%) were obtained as various aliphatic and aromatic amines (compounds **8a-r**, R^2 = alkyl, 4-MeC_6H_4, 2-MeC_6H_4 and 4-ClC_6H_4) were applied. The investigated functional groups (NO_2, COOEt, Cl, Br) are all tolerant for the one-pot method due to the mild reaction condition.



Scheme 3. Preparation of 2,3-dihydro-1*H*-2-benzazepin-1-ones **8**

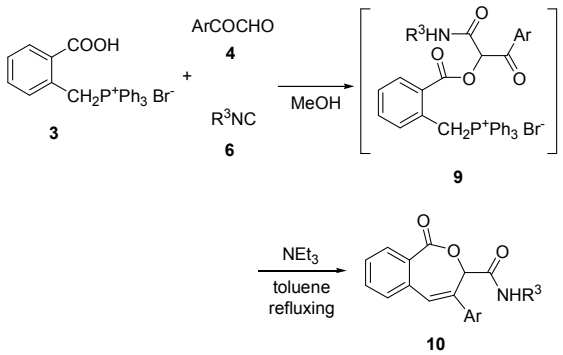
Table 2. Preparation of 2,3-dihydro-1*H*-2-benzazepin-1-ones **8**

	R^1	R^2	Ar	R^3	yield[b] (%)
8a	H	$PhCH_2$	4-ClC_6H_4	*t*-Bu	87

8b	H	Ph	4-ClC_6H_4	*t*-Bu	79
8c	H	*i*-Pr	4-ClC_6H_4	*t*-Bu	73
8d	H	*n*-Pr	4-ClC_6H_4	*t*-Bu	85
8e	H	$PhCH_2$	4-$CH_3C_6H_4$	*t*-Bu	87
8f	H	4-ClC_6H_4	4-ClC_6H_4	*t*-Bu	77
8g	H	$PhCH_2$	4-BrC_6H_4	*t*-Bu	72
8h	H	*n*-Bu	4-ClC_6H_4	*t*-Bu	75
8i	H	Et	4-ClC_6H_4	*t*-Bu	78
8j	H	4-$CH_3C_6H_4$	4-ClC_6H_4	*t*-Bu	81
8k	H	$PhCH_2$	4-$NO_2C_6H_4$	*t*-Bu	62
8l	H	$PhCH_2$	4-ClC_6H_4	*c*-C_6H_{11}	85
8m	H	Me	4-ClC_6H_4	*t*-Bu	81
8n	H	*n*-Pr	4-ClC_6H_4	*c*-C_6H_{11}	82
8o	H	*n*-Pr	4-$CH_3C_6H_4$	*t*-Bu	67
8p	H	4-$CH_3C_6H_4$	4-ClC_6H_4	*c*-C_6H_{11}	83
8q	H	2-$CH_3C_6H_4$	4-ClC_6H_4	*t*-Bu	74
8r	Br	$PhCH_2$	4-$CH_3C_6H_4$	*t*-Bu	75
8s	H	2-$MeOOCC_6H_4$	4-$CH_3C_6H_4$	*t*-Bu	52
8t	H	2-$MeOOCC_6H_4$	4-ClC_6H_4	*t*-Bu	56

[a]Isolated yields.

The Passerini reaction of phosphonium salt **3**, arylglyoxals **4** and isocyanide **6** also took place smoothly to give phosphonium intermediate **9**. In the presence of triethylamine, 3*H*-2-benzoxepin-1-ones **10** were obtained in good yields (70-86%, Table 3) via intramolecular Wittig reaction of **9** (Scheme 4). Various arylglyoxals can be used in above one-pot cyclization to prepare 3*H*-2-benzoxepin-1-ones **10** and good yields were reached regardless of the Ar group with substituents (Cl, Br, CH_3) on the benzene ring. A single crystal of **10a** was obtained from the CH_2Cl_2 solution, and X-ray structure analysis verified the proposed structure (Figure 1).



Scheme 4. Preparation of 3*H*-2-benzoxepin-1-ones **10**

Table 3. Preparation of 3*H*-2-benzoxepin-1-ones **10**

	Ar	R^3	Yield[a]
10a	4-ClC_6H_4	*t*-Bu	84
10b	4-ClC_6H_4	*c*-C_6H_{11}	76
10c	4-BrC_6H_4	*t*-Bu	85
10d	4-BrC_6H_4	*c*-C_6H_{11}	82
10e	Ph	*t*-Bu	78
10f	4-$CH_3C_6H_4$	*t*-Bu	86
10g	4-$CH_3C_6H_4$	*c*-C_6H_{11}	72
10h	4-BrC_6H_4	*n*-Bu	70

[a]Isolated yields.

In conclusion, the first example of I-MCR/Wittig sequence starting from phosphonium salt precursors for preparing heterocycles is reported. The method was adapted to the synthesis of various multisubstituted 2,3-dihydro-1*H*-2-benzazepin-1-ones and 3*H*-2-benzoxepin-1-ones in one-pot fashion. The used phosphonium salt acids, arylglyoxals, amines, and isocyanides can be varied broadly, producing products with multiple potential points of diversity, in combination to the easy availability of the synthetic approach and the large scope of the reaction makes it useful in synthetic and medicinal chemistry.

Experimental Section

Preparation of 2,3-dihydro-1*H*-2-benzazepin-1-ones 8

A mixture of phosphonium salt **3** (1 mmol), amine **5** (1 mmol), isocyanide **6** (1 mmol), and arylglyoxal **4** (1 mmol) was stirred in methanol (5 mL) at room temperature for 24-48 h, and then the solvent was evaporated under reduced pressure, NEt_3 (0.20 g, 2 mmol) with toluene (5 mL) was added to the reaction system and the reaction mixture was stirred at 110 ^oC for 2 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ether/petroleum ether = 1 : 4, V/V) to give **8**.

2-benzyl-N-(tert-butyl)-4-(4-chlorophenyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8a) White solid (yield 0.40 g, 87%), mp 184-186 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.04 (d, J = 7.8 Hz, 1H), 7.48-7.39 (m, 2H), 7.31-7.16 (m, 10H), 6.90 (s, 1H), 5.35 (s, 1H), 4.94 (d, J = 14.4 Hz, 1H), 4.86 (d, J = 13.8 Hz, 1H), 4.75 (s, 1H), 0.81 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.0, 166.5, 142.3, 138.8, 136.8, 133.9, 133.8, 133.7, 130.9, 129.4, 128.9, 128.8, 128.7, 128.6, 128.1, 127.8, 127.3, 127.1, 62.8, 53.6, 51.1, 27.8; MS (EI, 70 eV): m/z (%) = 458 (7) [M^+], 358 (55), 268 (25), 91 (100). Anal. Calcd for $C_{28}H_{27}ClN_2O_2$: C, 73.27; H, 5.93; N, 6.10. Found: C, 73.38; H, 5.67; N, 6.34.

N-(tert-butyl)-4-(4-chlorophenyl)-2-phenyl-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8b) Light yellow solid (yield 0.35 g, 79%), mp 166-168 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.08 (d, J = 7.8 Hz, 1H), 7.52-7.28 (m, 12H), 7.10 (s, 1H), 5.65 (s, 1H), 5.10 (s, 1H), 0.95 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.7, 166.3, 144.4, 142.0, 138.3, 134.5, 134.3, 133.8, 130.4, 129.6, 129.5, 129.3, 129.3, 128.8, 127.5, 127.2, 127.1, 126.7, 67.1, 51.6, 28.1; MS (EI, 70 eV): m/z (%) = 444 (18) [M^+], 344 (100), 316 (11), 242 (17), 178 (19), 104 (55). Anal. Calcd for $C_{27}H_{25}ClN_2O_2$: C, 72.88; H, 5.66; N, 6.30. Found: C, 72.92; H, 5.41; N, 6.57.

N-(tert-butyl)-4-(4-chlorophenyl)-2-isopropyl-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8c) White solid (yield 0.30 g, 73%), mp 235-237 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.98 (d, *J* = 7.8 Hz, 1H), 7.47-7.24 (m, 7H), 6.91 (s, 1H), 5.64 (s, 1H), 5.15-5.10 (m, 1H), 4.73 (s, 1H), 1.25 (d, *J* = 6.6 Hz, 3H), 0.93 (s, 9H), 0.83 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.6, 167.3, 143.1, 138.9, 134.6, 134.1, 133.7, 131.1, 130.7, 130.0, 129.1, 129.0, 128.3, 127.4, 57.5, 51.4, 46.2, 27.9, 21.9, 20.0; MS (EI, 70 eV): m/z (%) = 410 (14) [M^+], 310 (90), 268 (100), 241 (17), 178 (18). Anal. Calcd for $C_{24}H_{27}ClN_2O_2$: C, 70.15; H, 6.62; N, 6.82. Found: C, 69.92; H, 6.52; N, 6.98.

N-(tert-butyl)-4-(4-chlorophenyl)-2-propyl-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8d) White solid (yield 0.35 g, 85%), mp 155-158 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.98 (d, *J* = 7.8 Hz, 1H), 7.47-7.26 (m, 7H), 6.94 (s, 1H), 5.64 (s, 1H), 4.72 (s, 1H), 3.91-3.41 (m, 2H), 1.52-1.45 (m, 2H), 0.95 (s, 9H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.8, 166.7, 142.3, 139.0, 134.2, 134.1, 133.7, 131. 0, 130.7, 129.8, 129.0, 128.9, 128.2, 127.3, 64.1, 52.3, 51.3, 27.8, 21.8, 11.0; MS (EI, 70 eV): m/z (%) = 410 (10) [M^+], 310 (100), 268 (24). Anal. Calcd for $C_{24}H_{27}ClN_2O_2$: C, 70.15; H, 6.62; N, 6.82. Found: C, 70.33; H, 6.42; N, 6.89.

2-benzyl-N-(tert-butyl)-4-(p-tolyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8e) White solid (yield 0.38 g, 87%), mp 115-117 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.05 (d, *J* = 7.8 Hz, 1H), 7.45-7.11 (m, 12H), 6.93 (s, 1H), 5.32 (s, 1H), 4.92 (s, 2H), 4.81 (s, 1H), 2.36 (s, 3H), 0.80 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.2, 166.7, 143.2, 138.1, 137.4, 136.9, 134.4, 133.9, 131.3, 130.7, 129.4, 128.8, 128.7, 128.6, 127.8, 127.7, 125.7, 62.9, 53.6, 51.1, 27.7, 21.1; MS (EI, 70 eV): m/z (%) = 438 (12) [M^+], 338 (100), 248 (25), 91 (98). Anal. Calcd for $C_{29}H_{30}N_2O_2$: C, 79.42; H, 6.89; N, 6.39. Found: C, 79.69; H, 6.87; N, 6.58.

N-(tert-butyl)-2,4-bis(4-chlorophenyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8f) White solid (yield 0.37 g, 77%), mp 115-117 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.07 (d, *J* = 7.8

Hz, 1H), 7.53-7.31 (m, 11H), 7.12 (s, 1H), 5.55 (s, 1H), 5.04 (s, 1H), 0.93 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.6, 166.0, 143.0, 141.5, 137.9, 134.7, 134.0, 133.9, 133.0, 131.9, 131.2, 130.5, 129.5, 129.4, 128.8, 128.7, 128.3, 127.0, 66.9, 51.6, 27.9; MS (EI, 70 eV): m/z (%) = 478 (13) [M^+], 378 (100), 241 (34), 178 (30), 138 (64). Anal. Calcd for $C_{27}H_{24}Cl_2N_2O_2$: C, 67.65; H, 5.05; N, 5.84. Found: C, 67.84; H, 4.94; N, 5.89.

2-benzyl-4-(4-bromophenyl)-N-(tert-butyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8g) White solid (yield 0.36 g, 72%), mp 190-191 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.04 (d, *J* = 7.2 Hz, 1H), 7.46-7.09 (m, 12H), 6.90 (s, 1H), 5.35 (s, 1H), 4.95 (d, *J* = 13.8 Hz, 1H), 4.85 (d, *J* = 14.4 Hz, 1H), 4.74 (s, 1H), 0.81 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.0, 166.5, 142.4, 139.3, 136.8, 134.0, 133.8, 131.7, 131.2, 130.9, 129.6, 129.0, 128.9, 128.2, 128.0, 127.5, 122.1, 62.7, 53.5, 51.1, 27.7; MS (EI, 70 eV): m/z (%) = 502 (4) [M^+], 402 (36), 312 (14), 91 (100). Anal. Calcd for $C_{28}H_{27}BrN_2O_2$: C, 66.80; H, 5.41; N, 5.56. Found: C, 66.87; H, 5.21; N, 5.79.

N-(tert-butyl)-2-butyl-4-(4-chlorophenyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8h) White solid (yield 0.32 g, 75%), mp 101-103 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.98 (d, *J* = 7.8 Hz, 1H), 7.47-7.26 (m, 7H), 6.94 (s, 1H), 5.64 (s, 1H), 4.72 (s, 1H), 3.97-3.43 (m, 2H), 1.43-1.26 (m, 4H), 0.94 (s, 9H), 0.81 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.8, 166.7, 142.4, 139.0, 134.3, 134.2, 133.7, 131.0, 130.7, 129.8, 129.0, 128.9, 128.3, 127.3, 64.1, 51.4, 50.4, 30.6, 27.8, 19.7, 13.6; MS (EI, 70 eV): m/z (%) = 424 (9) [M^+], 324 (100), 268 (28). Anal. Calcd for $C_{25}H_{29}ClN_2O_2$: C, 70.66; H, 6.88; N, 6.59. Found: C, 70.88; H, 6.65; N, 6.74.

N-(tert-butyl)-4-(4-chlorophenyl)-2-ethyl-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8i) White solid (yield 0.31 g, 78%), mp 181-182 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.98 (d, *J* = 7.2 Hz, 1H), 7.47-7.26 (m, 7H), 6.94 (s, 1H), 5.64 (s, 1H), 4.73 (s, 1H), 3.91-3.58 (m, 2H), 1.13 (t, *J* = 7.2

Hz, 3H), 0.94 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.5, 166.7, 142.4, 138.9, 134.2, 133.7, 130.9, 130.7, 129.7, 129.1, 128.9, 128.3, 127.4, 64.0, 51.4, 45.7, 27.9, 13.9; MS (EI, 70 eV): m/z (%) = 396 (11) [M^+], 296 (100), 268 (20). Anal. Calcd for $C_{23}H_{25}ClN_2O_2$: C, 69.60; H, 6.35; N, 7.06. Found: C, 69.88; H, 6.25; N, 7.12.

N-(tert-butyl)-4-(4-chlorophenyl)-2-(p-tolyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8j) White solid (yield 0.37 g, 81%), mp 181-183 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.07 (d, *J* = 7.2 Hz, 1H), 7.50-7.18 (m, 11H), 7.09 (s, 1H), 5.66 (s, 1H), 5.07 (s, 1H), 2.35 (s, 3H), 0.95 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.7, 166.4, 142.0, 141.9, 138.3, 137.3, 134.4, 134.3, 133.8, 131.6, 131.0, 130.1, 130.0, 129.2, 128.7, 128.5, 127.1, 126.4, 67.1, 51.5, 27.9, 21.0; MS (EI, 70 eV): m/z (%) = 458 (16) [M^+], 358 (100), 330 (10), 242 (13), 178 (19), 118 (46). Anal. Calcd for $C_{28}H_{27}ClN_2O_2$: C, 73.27; H, 5.93; N, 6.10. Found: C, 73.13; H, 5.75; N, 6.36.

2-benzyl-N-(tert-butyl)-4-(4-nitrophenyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8k) Yellow solid (yield 0.29 g, 62%), mp 212-213 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.14 (d, *J* = 8.4 Hz, 2H), 8.05 (d, *J* = 7.2 Hz, 1H), 7.50-7.17 (m, 10H), 6.99 (s, 1H), 5.43 (s, 1H), 5.02 (d, *J* = 14.4 Hz, 1H), 4.78 (d, *J* = 13.8 Hz, 1H), 4.77 (s, 1H), 0.85 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.0, 166.3, 147.0, 146.7, 141.9, 136.8, 133.8, 133.4, 132.0, 131.2, 131.1, 129.4, 129.0, 128.9, 128.8, 128.2, 126.8, 123.9, 62.6, 53.4, 51.4, 27.8; MS (EI, 70 eV): m/z (%) = 469 (7) [M^+], 369 (42), 279 (51), 91 (100). Anal. Calcd for $C_{28}H_{27}N_3O_4$: C, 71.62; H, 5.80; N, 8.95. Found: C, 71.91; H, 5.87; N, 9.16.

2-benzyl-4-(4-chlorophenyl)-N-cyclohexyl-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8l) White solid (yield 0.41 g, 85%), mp 237-239 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.04 (d, *J* = 8.4 Hz, 1H), 7.45-7.14 (m, 12H), 6.91 (s, 1H), 5.40 (d, *J* = 8.4 Hz, 1H), 4.95 (d, *J* = 14.4 Hz, 1H), 4.84 (d, *J* = 13.8 Hz, 1H), 4.79 (s, 1H), 3.33-3.29 (m, 1H), 1.57-0.50 (m, 10H); ^{13}C NMR ($CDCl_3$, 150

MHz) δ (ppm) 168.2, 166.5, 141.9, 138.8, 136.8, 134.0, 133.5, 131.4, 131.1, 129.9, 129.1, 129.0, 128.9, 128.8, 128.3, 128.1, 127.1, 62.3, 53.5, 48.1, 32.3, 25.2, 24.5; MS (EI, 70 eV): m/z (%) = 484 (10) [M^+], 358 (98), 268 (32), 91 (100). Anal. Calcd for $C_{30}H_{29}ClN_2O_2$: C, 74.29; H, 6.03; N, 5.78. Found: C, 74.56; H, 6.17; N, 5.86.

N-(tert-butyl)-4-(4-chlorophenyl)-2-methyl-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8m) White solid (yield 0.31 g, 81%), mp 208-209 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.00 (d, *J* = 7.8 Hz, 1H), 7.47-7.26 (m, 7H), 6.97 (s, 1H), 5.55 (s, 1H), 4.74 (s, 1H), 3.36 (s, 3H,), 0.92 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.2, 166.5, 141.7, 139.0, 134.4, 134.1, 133.7, 131.1, 130.8, 129.9, 129.2, 128.8, 128.4, 127.2, 65.8, 51.4, 39.1, 27.9; MS (EI, 70 eV): m/z (%) = 382 (11) [M^+], 282 (100), 254 (15), 241 (20), 178 (20). Anal. Calcd for $C_{22}H_{23}ClN_2O_2$: C, 69.01; H, 6.05; N, 7.32. Found: C, 69.07; H, 5.81; N, 7.36.

4-(4-chlorophenyl)-N-cyclohexyl-2-propyl-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8n) White solid (yield 0.36 g, 82%), mp 111-112 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.98 (d, *J* = 7.8 Hz, 1H), 7.46-7.24 (m, 7H), 6.95 (s, 1H,), 5.68 (d, *J* = 7.8 Hz, 1H), 4.76 (s, 1H), 3.92-3.87 (m, 1H), 3.49-3.43 (m, 2H), 1.51-0.71 (m, 15H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.8, 166.6, 141.8, 139.0, 134.2, 133.9, 133.6, 131.1, 130.8, 130.1, 129.1, 129.0, 128.3, 127.3, 63.7, 52.3, 48.3, 32.3, 25.2, 24.6, 21.9, 11.1; MS (EI, 70 eV): m/z (%) = 436 (10) [M^+], 310 (100), 268 (22), 241 (10), 178 (10). Anal. Calcd for $C_{26}H_{29}ClN_2O_2$: C, 71.46; H, 6.69; N, 6.41. Found: C, 71.74; H, 6.74; N, 6.56.

N-(tert-butyl)-2-propyl-4-(p-tolyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8o) Yellow oil (yield 0.26 g, 67%), ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.00 (d, *J* = 7.8 Hz, 1H), 7.43-7.23 (m, 7H), 6.95 (s, 1H), 5.61 (s, 1H), 4.78 (s, 1H), 3.86-3.4 (m, 2H), 2.41 (s, 3H), 1.52-1.48 (m, 2H), 0.91 (s, 9H), 0.84 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 167.0, 143.1,

138.5, 137.5, 134.5, 134.1, 131.3, 130.6, 129.7, 128.9, 128.7, 128.0, 125.7, 64.3, 52.5, 51.3, 27.9, 21.8, 21.2, 11.1; MS (EI, 70 eV): m/z (%) = 390 (12) [M^+], 290 (100), 248 (16). Anal. Calcd for $C_{25}H_{30}N_2O_2$: C, 76.89; H, 7.74; N, 7.17. Found: C, 77.06; H, 7.53; N, 7.43.

4-(4-chlorophenyl)-N-cyclohexyl-2-(p-tolyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8p) White solid (yield 0.40 g, 83%), mp 196-197 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.06 (d, *J* = 7.2 Hz, 1H), 7.48-7.18 (m, 11H), 7.10 (s, 1H), 5.70 (d, *J* = 6.6 Hz, 1H), 5.12 (s, 1H), 3.50-3.45 (m, 1H), 2.35 (s, 3H), 1.54-0.62 (m, 10H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 166.5, 142.0, 141.5, 138.5, 137.4, 134.5, 134.1, 133.7, 131.7, 131.1, 130.4, 130.1, 129.3, 128.9, 128.7, 127.1, 126.4, 66.8, 48.4, 32.4, 25.2, 24.5, 21.1; MS (EI, 70 eV): m/z (%) = 484 (13) [M^+], 358 (100), 330 (9), 242 (10), 178 (17). Anal. Calcd for $C_{30}H_{29}ClN_2O_2$: C, 74.29; H, 6.03; N, 5.78. Found: C, 74.36; H, 6.21; N, 5.64.

N-(tert-butyl)-4-(4-chlorophenyl)-2-(o-tolyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8q) Light yellow solid (yield 0.34 g, 74%), mp 231-233 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.11 (d, *J* = 7.2 Hz, 0.7H), 8.02 (d, *J* = 7.2 Hz, 0.3H), 7.68-7.21 (m, 11H), 7.12 (s, 1H), 5.79 (s, 0.3H), 5.63 (s, 0.7H), 5.01 (s, 0.3H), 4.96 (s, 0.7H), 2.61 (s, 0.9H), 2.07 (s, 2.1H), 0.95 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 166.9, 166.3, 143.8, 142.1, 138.3, 135.2, 134.5, 134.2, 133.7, 131.9, 131.1, 130.6, 130.1, 129.3, 128.7, 128.6, 127.9, 127.6, 127.1, 126.9, 67.1, 51.5, 27.8, 18.1; MS (EI, 70 eV): m/z (%) = 458 (15) [M^+], 358 (100), 330 (9), 242 (18), 178 (22). Anal. Calcd for $C_{28}H_{27}ClN_2O_2$: C, 73.27; H, 5.93; N, 6.10. Found: C, 73.54; H, 5.87; N, 6.32.

2-benzyl-8-bromo-N-(tert-butyl)-4-(p-tolyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide

(8r) Light yellow solid (yield 0.39 g, 75%), mp 231-233 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.18 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.34-7.11 (m, 10H), 6.85 (s, 1H), 5.24 (s, 1H), 5.01 (d, *J* = 14.4 Hz, 1H), 4.82 (s, 1H), 4.77 (d, *J* = 14.4 Hz, 1H), 2.37 (s, 3H), 1.31 (s, 1H), 0.83 (s, 8H); ^{13}C NMR ($CDCl_3$,

150 MHz) δ (ppm) 166.9, 166.3, 143.8, 138.4, 137.2, 136.7, 135.5, 134.0, 133.7, 133.3, 130.4, 129.5, 128.9, 128.0, 127.5, 125.7, 121.7, 62.8, 53.6, 51.2, 27.8, 21.1; MS (EI, 70 eV): m/z (%) = 516 (8) [M^+], 418 (74), 326 (28), 189 (11), 91 (100). Anal. Calcd for $C_{29}H_{29}BrN_2O_2$: C, 67.31; H, 5.65; N, 5.41. Found: C, 67.18; H, 5.75; N, 5.20.

N-(tert-butyl)-2-(2-methoxycarbonylphenyl)-4-(p-tolyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8s) White solid (yield 0.25 g, 52%), mp 223-224 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.64 (s, 1H), 7.88-7.23 (m, 11H), 6.99 (s, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 5.33 (s, 1H), 3.99 (s, 3H), 2.41 (s, 3H), 1.03 (s, 8H), 0.93 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.7, 167.5, 166.8, 145.0, 143.1, 137.9, 137.8, 134.2, 134.0, 133.4, 130.7, 130.3, 129.6, 129.5, 128.9, 128.4, 128.0, 127.6, 126.7, 126.5, 126.4, 66.8, 52.7, 51.1, 27.9, 21.3; MS (EI, 70 eV): m/z (%) = 482 (2) [M^+], 382 (100), 351 (98), 322 (17), 221 (14), 162 (45), 130 (22). Anal. Calcd for $C_{30}H_{30}N_2O_4$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.84; H, 6.16; N, 5.66.

N-(tert-butyl)-4-(4-chlorophenyl)-2-(2-methoxycarbonylphenyl)-2,3-dihydro-1*H*-2-benzazepin-1-one-3-carboxamide (8t) White solid (yield 0.28 g, 56%), mp 235-237 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.68 (s, 1H), 7.90-7.29 (m, 11H), 7.00 (s, 1H), 6.76 (d, *J* = 6.6 Hz, 1H), 5.27 (s, 1H), 3.99 (s, 2.6H), 3.61 (s, 0.4H), 1.03 (s, 7.7H), 0.94 (s, 1.3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.5, 167.4, 166.6, 143.9, 143.0, 139.3, 134.0, 133.7, 133.5, 130.8, 130.4, 129.8, 129.0, 128.9, 128.0, 127.9, 126.9, 126.3, 66.7, 52.7, 51.2, 27.8; MS (EI, 70 eV): m/z (%) = 502 (1) [M^+], 403 (100), 371 (89), 342 (21), 241 (14), 162 (61), 130 (34). Anal. Calcd for $C_{29}H_{27}ClN_2O_4$: C, 69.25; H, 5.41; N, 5.57. Found: C, 69.01; H, 5.43; N, 5.46.

Preparation of 3*H*-2-benzoxepin-1-ones 10

A mixture of phosphonium salt **3** (1 mmol), isocyanide **6** (1 mmol), and arylglyoxal **4** (1 mmol) was stirred in methanol (5 mL) at room temperature for 48 h, and then the solvent was evaporated under reduced pressure, NEt_3 (0.20 g, 2 mmol) with toluene (5 mL) was added to the reaction system and the reaction mixture was stirred at 110 °C for 1-2 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ether/petroleum ether = 1 : 4, V/V) to give **10**.

N-(tert-butyl)-4-(4-chlorophenyl)-3*H*-2-benzoxepin-1-one-3-carboxamide (10a) White solid (yield 0.31 g, 84%), mp 163-164 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.96 (d, *J* = 7.8 Hz, 1H), 7.60-7.27 (m, 8H), 6.02 (s, 1H), 5.38 (s, 1H), 1.22 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 168.4, 165.1, 140.2, 135.2, 134.3, 133.9, 133.0, 132.5, 132.2, 131.0, 129.7, 129.3, 128.4, 127.4, 74.5, 51.7, 28.3; MS (EI, 70 eV): m/z (%) = 369 (4) [M^+], 270 (24), 230 (38), 174 (39), 157 (100). Anal. Calcd for $C_{21}H_{20}ClNO_3$: C, 68.20; H, 5.45; N, 3.79. Found: C, 68.49; H, 5.42; N, 3.90.

4-(4-chlorophenyl)-N-cyclohexyl-3*H*-2-benzoxepin-1-one-3-carboxamide (10b) White solid (yield 0.30 g, 76%), mp 209-212 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.93 (d, *J* = 7.8 Hz, 1H), 7.56-7.24 (m, 8H), 6.08 (s, 1H), 5.62 (d, *J* = 7.2 Hz, 1H), 3.75-3.69 (m, 1H), 1.88-0.93 (m, 10H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.5, 164.8, 139.4, 135.7, 134.3, 134.0, 133.0, 132.6, 131.1, 129.5, 128.6, 128.4, 127.4, 127.3, 74.5, 48.6, 32.6, 25.2, 24.6; MS (EI, 70 eV): m/z (%) = 395 (13) [M^+], 270 (31), 256 (100). Anal. Calcd for $C_{23}H_{22}ClNO_3$: C, 69.78; H, 5.60; N, 3.54. Found: C, 69.59; H, 5.43; N, 3.50.

4-(4-bromophenyl)-N-(tert-butyl)-3*H*-2-benzoxepin-1-one-3-carboxamide (10c) White solid (yield 0.35 g, 85%), mp 149-151 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.94 (d, *J* = 7.8 Hz, 1H), 7.57-7.25 (m, 8H), 6.00 (s, 1H), 5.48 (s, 1H), 1.23 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.5, 165.0, 140.1, 135.5, 134.9, 133.0, 132.6, 131.5, 131.4, 131.0, 129.7, 127.7, 127.6, 122.2, 74.5, 51.8, 28.2; MS

(EI, 70 eV): m/z (%) = 413 (1) [M^+], 371 (6), 314 (100). Anal. Calcd for $C_{21}H_{20}BrNO_3$: C, 60.88; H, 4.87; N, 3.38. Found: C, 60.83; H, 4.79; N, 3.64.

4-(4-bromophenyl)-N-cyclohexyl-3*H*-2-benzoxepin-1-one-3-carboxamide (10d) White solid (yield 0.36 g, 82%), mp 222-224 ^oC; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.93 (d, *J* = 7.8 Hz, 1H), 7.57-7.23 (m, 8H), 6.06 (s, 1H), 5.57 (d, *J* = 7.2 Hz, 1H), 3.73-3.69 (m, 1H), 1.88-0.92 (m, 10H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.5, 164.8, 139.4, 135.9, 134.8, 132.9, 132.6, 131.5, 131.4, 131.1, 129.8, 127.7, 127.6, 122.2, 74.5, 48.7, 32.6, 25.3, 24.7; MS (EI, 70 eV): m/z (%) = 439 (11) [M^+], 314 (19), 299 (15), 256 (100). Anal. Calcd for $C_{23}H_{22}BrNO_3$: C, 62.74; H, 5.04; N, 3.18. Found: C, 62.84; H, 4.91; N, 3.35.

N-(tert-butyl)-4-phenyl-3*H*-2-benzoxepin-1-one-3-carboxamide (10e) White solid (yield 0.26 g, 78%), mp 167-169 ^oC; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.96 (d, *J* = 7.8 Hz, 1H), 7.58-7.28 (m, 9H), 6.04 (s, 1H), 5.36 (s, 1H), 1.15 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.7, 164.4, 140.4, 136.9, 136.6, 135.8, 133.4, 132.4, 132.3, 130.0, 128.8, 128.6, 125.9, 125.6, 75.0, 51.6, 28.3; MS (EI, 70 eV): m/z (%) = 335 (4) [M^+], 236 (32), 230 (42), 174 (45), 157 (100). Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.49; H, 6.20; N, 4.17.

N-(tert-butyl)-4-(p-tolyl)-3*H*-2-benzoxepin-1-one-3-carboxamide (10f) White solid (yield 0.30 g, 86%), mp 136-138 ^oC; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.96 (d, *J* = 6.0 Hz, 1H), 7.58-7.13 (m, 8H), 6.00 (s, 1H), 5.35 (s, 1H), 2.31 (s, 3H), 1.15 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 168.7, 164.4, 140.4, 138.2, 136.7, 133.5, 132.7, 132.4, 132.3, 131.2, 129.9, 129.4, 129.3, 125.8, 75.0, 51.6, 28.2, 21.0; MS (EI, 70 eV): m/z (%) = 349 (11) [M^+], 276 (15), 250 (32), 230 (46), 174 (52) 157 (100), 119 (47). Anal. Calcd for $C_{22}H_{23}NO_3$: C, 75.62; H, 6.63; N, 4.01. Found: C, 75.55; H, 6.41; N, 4.27.

N-cyclohexyl-4-(p-tolyl)-3*H*-2-benzoxepin-1-one-3-carboxamide (10g) White solid (yield 0.27 g,

72%), mp 128-130 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.94 (d, *J* = 7.6 Hz, 1H), 7.54 (s, 2H), 7.54-7.09 (m, 8H), 6.07 (s, 1H), 5.64 (d, *J* = 6.8 Hz, 1H), 3.70-3.66 (m, 1H), 2.29 (s, 3H), 1.93-0.81 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 168.8, 164.4, 139.6, 138.2, 136.9, 133.4, 132.6, 132.4, 132.3, 131.3, 129.9, 129.4, 129.3, 125.8, 75.0, 48.5, 32.3, 25.3, 24.6, 21.0; MS (EI, 70 eV): m/z (%) = 375 (48) [M^+], 292 (24), 276 (31), 250 (47), 233 (100). Anal. Calcd for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.73. Found: C, 76.94; H, 6.45; N, 3.93.

4-(4-bromophenyl)-N-butyl-3*H*-2-benzoxepin-1-one-3-carboxamide (10h) White solid (yield 0.29 g, 70%), mp 176-178 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.04 (d, *J* = 7.8 Hz, 1H), 7.66-7.27 (m, 7H), 6.99 (s, 1H), 6.90 (s, 1H), 5.31 (s, 1H), 3.32-3.11 (m, 2H), 1.43-1.25 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 167.9, 165.7, 141.5, 136.6, 135.0, 134.1, 132.9, 132.4, 131.5, 129.6, 129.5, 128.9, 128.6, 122.5, 75.4, 39.0, 31.3, 19.9, 13.6; MS (EI, 70 eV): m/z (%) = 413 (1) [M^+], 371 (13), 314 (100), 286 (44). Anal. Calcd for $C_{21}H_{20}BrNO_3$: C, 60.88; H, 4.87; N, 3.38. Found: C, 60.94; H, 4.78; N, 3.60.

Isolation of phosphonium intermediate 7e

A mixture of phosphonium salt **3a** (0.48 g, 1 mmol), benzylamine (0.12 g, 1.1 mmol), *t*-butylisocyanide (0.09 g, 1.1 mmol), and *p*-tolylglyoxal (0.16 g, 1.1 mmol) was stirred in methanol (5 mL) at room temperature for 48 h, and then the solvent was evaporated under reduced pressure. The residue was washed three times with ether/petroleum ether (1:1, 10 mL×3) and then recrystallized from methanol/ether (1:2) to give the phosphonium intermediate **7e** as white solid (yield 0.41 g, 51%), mp 191-193 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm) 8.42 (s, 1H), 7.91-7.01 (m, 28H), 6.10 (s, 1H), 5.22 (d, *J* = 14.4 Hz, 2H), 4.00-3.94 (m, 2H), 2.40 (s, 3H), 0.98 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ

(ppm) 191.9, 170.4, 163.6, 144.0, 136.9, 136.4, 135.6, 135.2, 134.1, 132.7, 130.6, 130.2, 130.1, 129.9, 129.2, 128.5, 128.3, 127.8, 127.3, 127.1, 126.1, 125.9, 118.5, 117.7, 65.3, 50.7, 39.5, 27.5, 21.2; MS (EI, 70 eV): m/z (%) = 717 (37) [M^+-Br^-], 381 (86), 322 (63), 256 (100), 211 (64), 120 (72). Anal. Calcd for $C_{47}H_{46}BrN_2O_3P$: C, 70.76; H, 5.81; N, 3.51. Found: C, 70.53; H, 5.69; N, 3.60.

Isolation of phosphonium intermediate 9a

A mixture of phosphonium salt **3a** (0.48 g, 1 mmol), *t*-butylisocyanide (0.09 g, 1.1 mmol), and 4-chlorophenylglyoxal (0.19 g, 1.1 mmol) was stirred in methanol (5 mL) at room temperature for 48 h, and then the solvent was evaporated under reduced pressure. The residue was washed three times with ether/petroleum ether (1:1, 10 mL×3) and then recrystallized from methanol/ether (1:2) to give the phosphonium intermediate **9a** as white solid (yield 0.31 g, 43%), mp 178-179 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ (ppm) 8.36 (s, 1H), 8.03-7.18 (m, 23H), 6.27 (s, 1H), 5.63-5.49 (m, 2H), 1.22 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 189.5, 164.7, 162.1, 139.0, 135.0, 133.9, 133.8, 132.3, 130.5, 130.1, 130.0, 129.8, 129.2, 129.1, 128.9, 128.8, 128.1, 125.2, 117.8, 116.9, 77.6, 51.1, 39.5, 27.7; MS (EI, 70 eV): m/z (%) = 727 (13) [M^+], 370 (8), 278 (100), 238 (40), 174 (37), 139 (26). Anal. Calcd for $C_{39}H_{36}BrClNO_4P$: C, 64.25; H, 4.98; N, 1.92. Found: C, 64.45; H, 4.76; N, 1.97.

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Supporting Information

^{1}H and ^{13}C NMR spectra of compounds **8**, **7e**, **9a** and **10**, X-ray crystallographic data (CIF file) of compound **10a**, This material is available free of charge via the Internet at http://pubs.acs.org.

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