DOI 10.1007/s10593-018-2322-y

*Chemistry of Heterocyclic Compounds* **2018**, *54*(6), 650–657

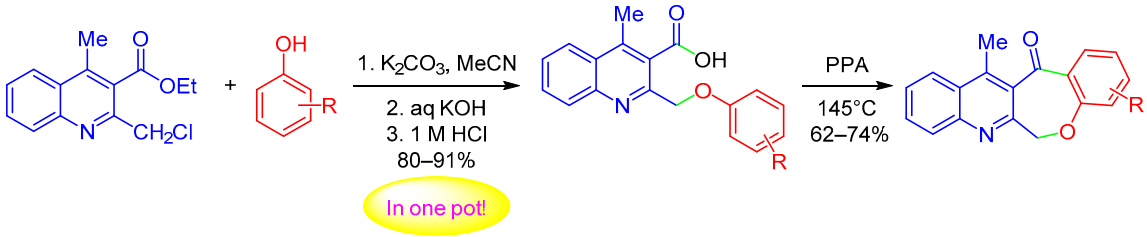
# Convenient synthesis of 12-methyl[1]benzoxepino-[3,4-*b*]quinolin-13(6*H*)-ones

**Yu Wang[1], Mingqin Chang[1], Hong Zhang[1], Yang Li[1]***

[1] *Institute of Superfine Chemicals, Bohai University, Jinzhou 121000, China; e-mail: bhuzh@163.com*

Published in Khimiya Geterotsiklicheskikh Soedinenii, 2018, *54*(6), 650–657

Submitted January 20, 2018
Accepted after revision April 17, 2018




In this work, a construction of 12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-ones, structurally intriguing hybrid molecules consisting of fused 4-methylquinoline and 1-benzoxepin-5-one units, has been successfully achieved *via* a two-step procedure, involving the one-pot synthesis of 2-(aryloxymethyl)-4-methylquinoline-3-carboxylic acids followed by their intramolecular Friedel–Crafts cyclization reaction. Our synthetic protocol described here could be attractive as it is simple, easy to handle and does not involve the use of expensive reagents or catalysts.

**Keywords**: 1-benzoxepin-5-one, hybrid molecule, 4-methylquinoline, Friedel–Crafts cyclization, one-pot synthesis.

1-Benzoxepine ring is one of the privileged medicinal scaffolds found in a small number of biologically active natural products, such as pterulone (**1**),[1] ptaeroxylin (**2**),[2] and bauhiniastatins (e.g., bauhiniastatin 1 (**3**))[3] (Fig. 1), and has wide application in the design and discovery of novel bioactive molecules.[4,5] Many compounds containing the 1-benzoxepine core are of great pharmaceutical interest due to their potent biological properties, such as antimycobacterial, anticancer,[6] and antifungal activities,[7] and could be potentially applied as topoisomerase I,[8] cyclooxygenase,[9] and PI3-kinase inhibitors.[10] As a consequence, considerable synthetic efforts have been devoted surrounding the 1-benzoxepine template for further modification and functionalization by both organic and medicinal chemists with the aim of enhancing the potency of this class of compounds.[11–13]

On the other hand, the 4-methylquinoline (4-MeQ) scaffold, too, is a pharmacologically significant structural unit, and many 4-methylquinoline-based heterocyclic compounds have been used as drug-like chemical probes in pharmacological studies or for the development of new medicinal products.[14,15] For example, 4-methyl-2-phenylquinoline (**4**) was reported to show potent inhibitory effects against β(1–3) glucan synthase with lower $IC_{50}$ value

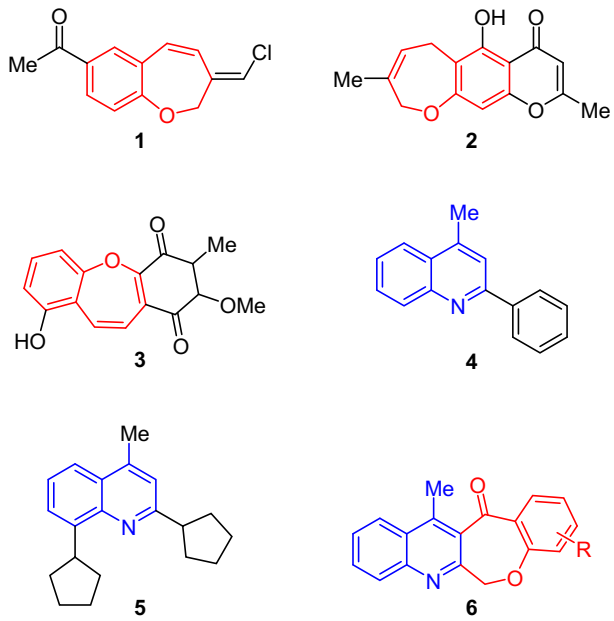
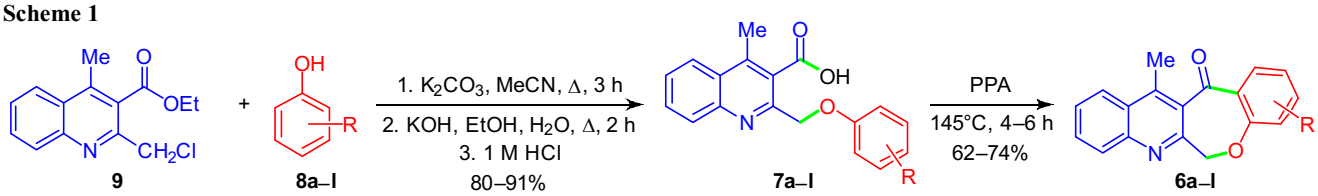



**Figure 1**. Structures of 1-benzoxepine-containing natural products **1**–**3**, bioactive 4-methylquinolines **4**, **5**, and the target hybrid molecules **6**.

**Scheme 1**




(0.23 μg/ml) than the well-known β(1–3) glucan synthase inhibitor aculeacin A ($IC_{50}$ 50.5 μg/ml).[16] In this regard, Jain et al.[17] have described the synthesis and anti-tuberculosis activity of a series of ring-substituted 4-methylquinolines, such as 2,8-dicyclopentyl-4-methyl-quinoline (**5**), and established that these molecules could be regarded as promising lead compounds for antituberculosis drug development. Due to their biological activities, interest in the synthesis of novel and interesting types of 4-methylquinoline-based derivatives continues unabated.[18,19]

On the basis of the literature data, and considering the fact that combination of different pharmacophores in a molecular framework is an important goal of synthetic organic chemistry and plays a prominent role in modern drug discovery,[20] we felt that it would be a worthwhile endeavor to construct 4-methylquinoline–1-benzoxepine fused hybrids as possible drug candidates for current pharmacological studies. Accordingly, with this context and in continuation of our studies concerning the synthesis of novel and potential biologically active quinoline-based heterocycles,[21–25] we herein would like to report the design and synthesis of 4-methylquinoline-based 1-benzoxepine derivatives, wherein the 1-benzoxepine ring is fused at its 3 and 4 positions to the *b* position of the 4-methylquinoline ring to give a tetracyclic structure exemplified by compounds **6** as shown in Figure 1.

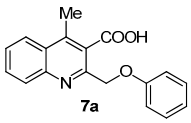
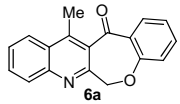
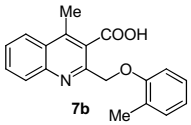
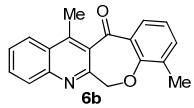
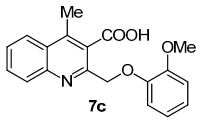
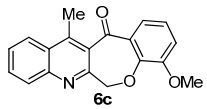
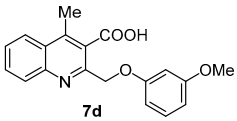
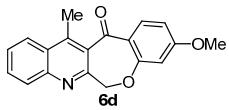
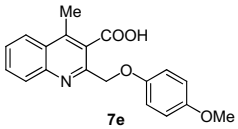
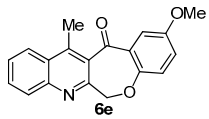
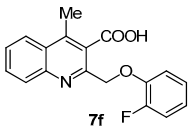
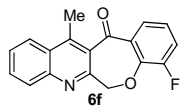
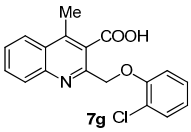
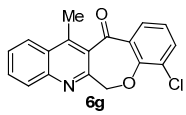
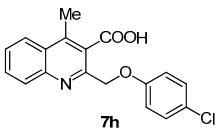
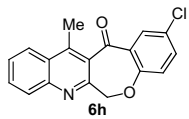
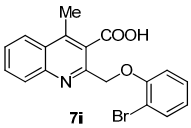
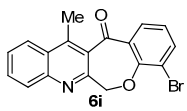
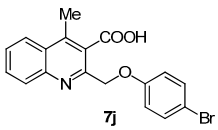
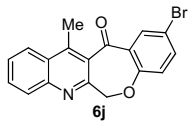
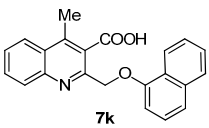
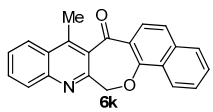
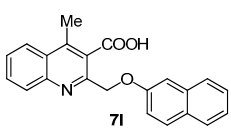
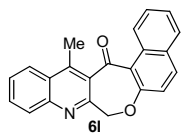
Prior to the current investigation, there have been few reports concerning the synthesis of ethyl 2-chloromethyl-4-methylquinoline-3-carboxylate (**9**) through the Friedländer annulation reaction.[26,27] Although the compound could be considered as a useful building block to participate in a wide array of chemical transformations for the design of new and interesting quinoline derivatives, to our knowledge, the further modification of it has been very limited so far. In this regard, Degtyarenko et al.[28] reported its synthetic application with amines or mercaptanes for the synthesis of 4-methylquinoline-based derivatives. Just recently, Xu et al.[29] reported the reaction of compound **9** with salicylonitriles or 2-mercaptobenzonitrile for the facile synthesis of benzofuran- or benzothiophene-fused naphthyridines. Due to structural diversity being an essential component of the search for new leads, we became interested in exploring the further synthetic application of compound **9** as an ideal starting material for facile synthesis of the desired 4-methylquinoline-based 1-benzoxepine derivatives. Our synthetic plan, as shown in Scheme 1, was to make use of the active 2-chloromethyl group of compound **9** to generate 2-aryloxymethyl moiety through Williamson ether reaction with substituted phenols **8** followed by a further *in situ* ethyl ester hydrolysis reaction at position 3 to afford the corresponding 2-aryloxymethylquinoline-3-carboxylic acid intermediates **7**. Subsequently, the intramolecular Friedel–Crafts cyclization reaction between 2-aryloxymethyl moiety and 3-carboxylic acid group would construct the desired 1-benzoxepine skeleton through the generation of a new C–C bond.

Accordingly, with this assumption in mind, starting compound **9** obtained by the described method[27] was first subjected to the Williamson reaction with 1.1 equiv of phenols **8a**–**l** in the presence of $K_2CO_3$ as the base and refluxing MeCN as the solvent. The reaction proceeded very smoothly, and the substrates were completely consumed within 3 h as monitored by TLC. It is worthy to mention that the reaction proceeded also in DMF as the solvent. We adopted herein MeCN as the solvent of choice simply because of its low boiling point, thus bringing much convenience to subsequent work-up procedure. Since the resulting aryloxymethyl ethers from the Williamson reaction did not interfere with further ethyl ester hydrolysis reaction, purification at this stage was unnecessary. As such, we simply evaporated MeCN to dryness, added aqueous-ethanolic potassium hydroxide solution directly to the residue, and continued to reflux for additional 2 h. After an acidic work-up followed by purification of the resulting crude products by recrystallization from ethanol, the corresponding 2-aryloxymethylquinoline-3-carboxylic acids **7a**–**l** were obtained in high yields as listed in Table 1.

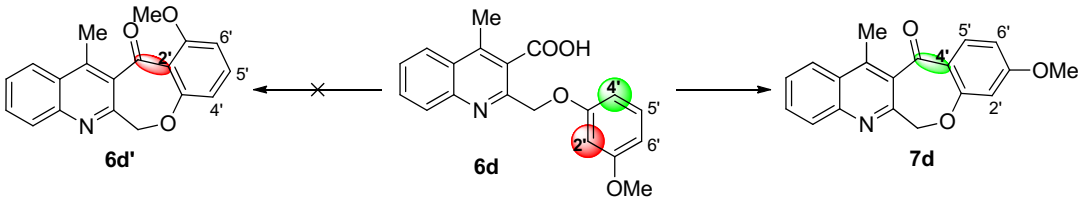
To the best of our knowledge, these newly synthesized compounds except compound **7a**[30] have not been reported earlier, and their structures have been confirmed based on their spectroscopic and analytical data which are in good agreement with the proposed structures (see Experimental). As an example, the $^1$H NMR spectrum of compound **7a** did not show signals attributable to chloromethyl and ethoxy protons of its precursor **9**, but instead contained a one-proton singlet at 13.61 ppm and a two-proton singlet at 5.36 ppm, readily recognizable as arising from carboxylic and methylene protons, respectively. Moreover, the presence of a total of 9 aromatic protons in the range of 6.95–8.20 ppm exactly matches its structure as well. Further, the structure of compound **7a** was confirmed by its $^{13}$C NMR spectrum, which revealed the presence of carboxyl carbon at 168.7 ppm and methylene carbon at 70.5 ppm, along with the signals due to the aromatic carbons. The other synthesized compounds exhibited similar spectral characteristics but for the substituents which were recognized by characteristic signals with appropriate chemical shifts.

Having a series of the synthesized precursors **7a**–**l** in hand, our attention was turned to their intramolecular Friedel–Crafts cyclization reaction for construction of the tetracyclic title compounds. In our first attempts to carry out the transformation of carboxylic acid **7a** into benzoxepino-

**Table 1**. Yields and physical properties of compounds **7a**–**l** and **6a**–**l**

| Entry | Carboxylic acids | Mp, °C | Yield, % | Benzoxepinoquinolinones | Mp, °C | Yield, % |
|---|---|---|---|---|---|---|
| 1 |  **7a** | 210–212 (217–219°C)[30] | 87 |  **6a** | 217–218 | 72 |
| 2 |  **7b** | 197–199 | 82 |  **6b** | 206–207 | 65 |
| 3 |  **7c** | 213–214 | 80 |  **6c** | 201–201 | 62 |
| 4 |  **7d** | 192–194 | 86 |  **6d** | 218–219 | 69 |
| 5 |  **7e** | 184–186 | 91 |  **6e** | 227–228 | 74 |
| 6 |  **7f** | 195–197 | 83 |  **6f** | 228–229 | 63 |
| 7 |  **7g** | 207–208 | 86 |  **6g** | 213–215 | 66 |
| 8 |  **7h** | 210–211 | 88 |  **6h** | 238–239 | 71 |
| 9 |  **7i** | 198–199 | 84 |  **6i** | 240–242 | 63 |
| 10 |  **7j** | 190–192 | 82 |  **6j** | 249–251 | 69 |
| 11 |  **7k** | 213–214 | 89 |  **6k** | 251–252 | 70 |
| 12 |  **7l** | 227–228 | 87 |  **6l** | 242–244 | 72 |

**Scheme 2**




quinolinone **6a** using Eaton's reagent as the mild cyclization reagent at 80°C,[31] the reaction scarcely proceeded and the desired product **6a** was detected only in negligible amount that did not warrant isolation. We also tried the reaction using $POCl_3$ as the cyclization reagent, which has recently been used for this type of transformation.[32] However, this purported approach was ineffective in our hands and the reaction did not proceed satisfactorily, giving poor yields of highly impure products. In addition, switching to other cyclization reagents, such as sulfuric acid, hydrogen fluoride, and trifluoroacetic anhydride, was also to no avail.

After these fruitless attempts, we were delight to find that the use of polyphosphoric acid (PPA)[21] was suitable to promote the reaction, and the reaction temperature of 145°C was found to be optimal to complete the transformation, giving compound **6a** in a good yield of 72%. Upon further increasing the reaction temperature, the crude product was always contaminated with a small amount of impurities, which may be attributed to side reactions, such as polymerization. Due to the simplicity of the procedure requiring no additional solvent, no further optimization in reaction conditions was necessary and the above-mentioned conditions were chosen for the following work. Thereafter, in a similar fashion, we further extended the reaction to other quinoline-3-carboxylic acids **7b**–**l**. As expected, these substrates were equally amenable to the reaction process without any experimental difficulties, successfully furnishing the corresponding targeted products **6b**–**l** in satisfactory yields. The results of this series of experiments are compiled in Table 1.

The newly synthesized compounds **6a**–**l** have never been reported, and their structures were all easily established based on their spectral data and elemental analyses, which were in good agreement with the proposed structures (see Experimental). In particular, we would like to comment on the intramolecular cyclization of compounds **7d** and **7l** (entries 4 and 12, Table 1). In the case of compound **7d**, the intramolecular cyclization reaction in principle should give rise to two possible structural isomers **6d** and **6d'** because of the existence of two vacant *ortho* sites, C-2' and C-4', in the 3-methoxyphenyl group of compound **6d**. But in fact, the $^1$H NMR spectrum of the product suggested that the cyclization reaction selectively occurred with the C–C bond forming at the C-4' position, thereby affording structure **6d** as the sole product as shown in Scheme 2.

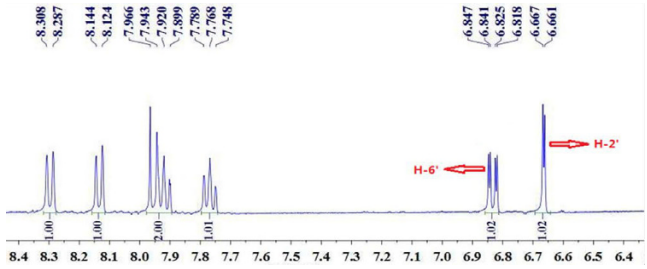



**Figure 2**. The $^1$H NMR spectrum of compound **6d**.

In the $^1$H NMR spectrum of compound **6d** (Fig. 2), particularly characteristic was the signal due to the C-2' hydrogen appeared as a doublet at 6.66 ppm with a small coupling constant $J$ = 2.4, which is a typical value for *meta*-proton coupling with C-6' hydrogen. Correspondingly, the signal due to C-6' hydrogen appears as a doublet of doublets at 6.83 ppm with the $J$ values 8.8 and 2.4 Hz which arose from coupling with both C-5' and C-2' hydrogen atoms. If the cyclization reaction occurred at the C-2' position leading to the corresponding product **6d'**, the splitting pattern of *meta*-proton coupling doublet could not appear in its $^1$H NMR spectrum.

Similarly, the cyclization reaction of acid **7l** could also occur theoretically at either a- or b-position of the naphthalene ring, resulting in two possible structural isomers. However, the analysis of $^1$H NMR spectrum revealed that the cyclization reaction selectively took place at the a-position of the naphthalene ring to give product **6l** as the sole product as shown in Scheme 3.

The $^1$H NMR spectrum of compound **6l** (Fig. 3) exhibited two doublet signals that can be assigned to H-b and H-c at 7.22 and 7.95 ppm with a coupling constant $J$ = 8.8,

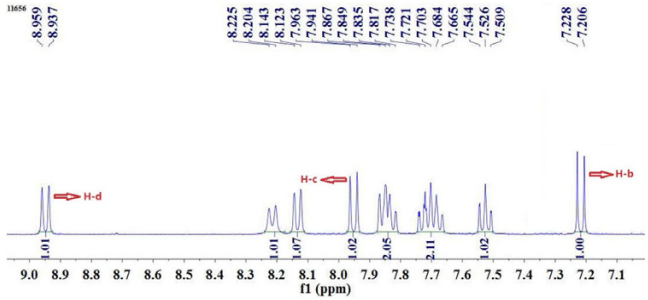
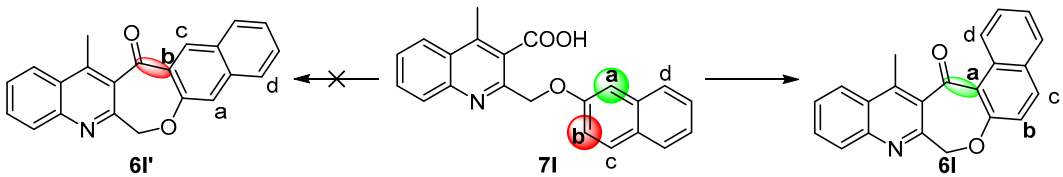



**Figure 3**. The $^1$H NMR spectrum of compound **6l**.

**Scheme 3**



which is a typical value for *ortho*-protons coupling in naphthalene ring. Especially, the one-proton doublet at markedly high $\delta_H$ value (8.95 ppm) could be easily ascribed to H-d due to the intramolecular interaction between the carbonyl oxygen atom and this proton resulting in the downfield shift. Further, if the cyclization reaction occurred at the C-b position giving compound **6l'** as the product, there should have been two one-proton singlet signals due to H-a and H-c in its $^1$H NMR spectrum.

In conclusion, we have provided an easy access to structurally new and biologically promising polycyclic fused 4-methylquinoline-based 1-benzoxepine derivatives through a simple and effective two-step procedure. In view of the synergism of both the 1-benzoxepine ring and 4-methylquinoline unit in a molecular framework, these newly synthesized compounds would likely possess significant biological activities and might be potentially applied for the development of biologically and pharmaceutically important drugs. Currently, the studies concerning their application are underway.

## Experimental

Infrared spectra were recorded on a Shimadzu FTIR-8400S spectrophotometer in KBr pellets in the range of 400–4000 cm$^{-1}$. $^1$H and $^{13}$C NMR spectra were recorded on a Brucker Avance NMR spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ (compounds **6a**,**b**,**e**,**g**–**l**) or in DMSO-$d_6$ (compounds **6c**,**d**,**f**, **7a**–**l**). The reported chemical shift (δ) values are given in parts per million downfield from TMS as the internal standard. Elemental analyses were performed for C, H, and N using an Elementar vario EL III element analyzer. Melting points were determined using a WRS-1B melting point apparatus. The progress of reactions was monitored by thin-layer chromatography (TLC) on silica gel GF254 using EtOAc – petroleum ether as eluent. The chemicals used in this work were obtained from Fluka and were used without further purification.

**Synthesis of 2-(aryloxymethyl)-4-methylquinoline-3-carboxylic acids 7a–l** (General method). Phenol or substituted phenol **8a**–**l** (1.1 mmol) and anhydrous $K_2CO_3$ (415 mg, 3 mmol) were added to a stirred solution of ethyl 2-(chloromethyl)-4-methylquinoline-3-carboxylate **9** (264 mg, 1 mmol) in MeCN (15 ml). The resulting mixture was heated at refluxing temperature for 3 h. The conversion was monitored by TLC. After completion, the reaction mixture was evaporated to dryness; a solution of KOH (1.12 g, 20 mmol) in 80% ethanol (25 ml) was added directly to the residue and the reflux was continued for 2 h. After cooling, the reaction mixture was acidified to pH 4–5 with 1 M HCl to induce precipitation. After filtration and washing with water, the crude precipitate was recrystallized from ethanol. The yields and melting points of products **7a**–**l** are listed in Table 1.

**4-Methyl-2-(phenoxymethyl)quinoline-3-carboxylic acid (7a)**. White solid. IR spectrum, ν, cm$^{-1}$: 3442 (COOH), 3075, 2961, 1721 (C=O), 1600, 1569, 1490. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.71 (3H, s, $CH_3$); 5.36 (2H, s, $ArCH_2O$); 6.95 (1H, t, *J* = 7.2, H Ar); 7.02 (2H, d, *J* = 8.0, H Ar); 7.29 (2H, t, *J* = 8.0, H Ar); 7.71 (1H, t, *J* = 7.6, H Ar); 7.84 (1H, t, *J* = 7.6, H Ar); 8.05 (1H, d, *J* = 8.0, H Ar); 8.20 (1H, d, *J* = 8.4, H Ar); 13.61 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.1; 70.5; 114.4; 120.8; 124.5; 126.2; 127.2; 127.5; 129.0; 129.2; 130.1; 141.8; 145.4; 152.6; 157.8; 168.7. Found, %: C 73.92; H 5.00; N 4.62. $C_{18}H_{15}NO_3$. Calculated, %: C 73.71; H 5.15; N 4.78.

**4-Methyl-2-[(*o*-tolyloxy)methyl]quinoline-3-carboxylic acid (7b)**. White solid. IR spectrum, ν, cm$^{-1}$: 3447 (COOH), 3059, 2919, 1724 (C=O), 1610, 1572, 1508. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.16 (3H, s, $CH_3$); 2.72 (3H, s, $CH_3$); 5.38 (2H, s, $ArCH_2O$); 6.83 (1H, t, *J* = 7.2, H Ar); 7.05 (1H, d, *J* = 8.0, H Ar); 7.10–7.14 (2H, m, H Ar); 7.73 (1H, t, *J* = 7.2, H Ar); 7.86 (1H, t, *J* = 7.2, H Ar); 8.08 (1H, d, *J* = 8.4, H Ar); 8.22 (1H, d, *J* = 8.4, H Ar); 13.55 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.2; 15.7; 70.3; 110.7; 120.2; 124.6; 125.8; 126.3; 126.5; 127.3; 127.4; 128.8; 130.2; 130.3; 142.3; 145.2; 152.7; 155.9; 168.6. Found, %: C 74.41; H 5.68; N 4.27. $C_{19}H_{17}NO_3$. Calculated, %: C 74.25; H 5.58; N 4.56.

**2-[(2-Methoxyphenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7c)**. White solid. IR spectrum, ν, cm$^{-1}$: 3430 (COOH), 3077, 2963, 1718 (C=O), 1616, 1569, 1506. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.76 (3H, s, $CH_3$); 3.77 (3H, s, $OCH_3$); 5.36 (2H, s, $ArCH_2O$); 6.86 (1H, td, *J* = 7.6, *J* = 1.2, H Ar); 6.94 (1H, td, *J* = 7.6, *J* = 1.2, H Ar); 7.00 (1H, dd, *J* = 7.6, *J* = 1.2, H Ar); 7.10 (1H, dd, *J* = 7.6, *J* = 1.2, H Ar); 7.74 (1H, t, *J* = 7.6, H Ar); 7.87 (1H, t, *J* = 7.6, H Ar); 8.07 (1H, d, *J* = 8.4, H Ar); 8.24 (1H, d, *J* = 8.4, H Ar); 13.60 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.2; 55.3; 71.3; 112.2; 114.1; 120.3; 121.5; 124.5; 126.2; 127.3; 127.6; 129.0; 130.2; 142.0; 145.4; 147.5; 149.2; 152.5; 168.6. Found, %: C 70.93; H 5.07; N 4.09. $C_{19}H_{17}NO_4$. Calculated, %: C 70.58; H 5.30; N 4.33.

**2-[(3-Methoxyphenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7d)**. White solid. IR spectrum, ν, cm$^{-1}$: 3405 (COOH), 3058, 2871, 1716 (C=O), 1614, 1575, 1487. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.84 (3H, s, $CH_3$); 3.84 (3H, s, $OCH_3$); 5.48 (2H, s, $ArCH_2O$); 6.66 (1H, dd, *J* = 8.0, *J* = 1.6, H Ar); 6.71 (1H, d, *J* = 7.6, H Ar); 6.74 (1H, d, *J* = 1.6, H Ar); 7.31 (1H, t, *J* = 8.0, H Ar); 7.84 (1H, t, *J* = 7.6, H Ar); 7.97 (1H, t, *J* = 7.6, H Ar); 8.18 (1H, d, *J* = 8.4, H Ar); 8.33 (1H, d, *J* = 8.4, H Ar); 13.72 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.1; 54.7; 70.6; 100.8; 106.4; 106.7; 124.5; 126.2; 127.2; 127.5; 129.0; 129.6; 130.2; 141.8; 145.4; 152.6; 159.1; 160.1; 168.7. Found, %: C 70.35; H 5.58; N 4.17. $C_{19}H_{17}NO_4$. Calculated, %: C 70.58; H 5.30; N 4.33.

**2-[(4-Methoxyphenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7e)**. White solid. IR spectrum, ν, cm$^{-1}$: 3441 (COOH), 3058, 2923, 1727 (C=O), 1616, 1558, 1509. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, $CH_3$); 3.67 (3H, s, $OCH_3$); 5.30 (2H, s, $ArCH_2O$); 6.85 (2H, d, *J* = 8.8, H Ar); 6.95 (2H, d, *J* = 8.8, H Ar); 7.71 (1H, t, *J* = 7.6, H Ar); 7.84 (1H, t, *J* = 7.6, H Ar); 8.04 (1H, d, *J* = 8.0, H Ar); 8.20 (1H, d, *J* = 8.4, H Ar); 13.58 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.0; 55.0; 71.2; 114.2; 115.5; 124.5; 126.2; 127.2; 127.5; 129.0; 130.1; 141.7; 145.4; 151.8; 152.9; 153.4; 168.7. Found, %: C 70.37; H 5.07; N 4.49. $C_{19}H_{17}NO_4$. Calculated, %: C 70.58; H 5.30; N 4.33.

**2-[(2-Fluorophenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7f)**. White solid. IR spectrum, ν, $cm^{-1}$: 3384 (COOH), 3066, 2918, 1718 (C=O), 1646, 1592, 1503. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.72 (3H, s, $CH_3$); 5.43 (2H, s, $ArCH_2O$); 6.92–6.97 (1H, m, H Ar); 7.09 (1H, t, *J* = 8.0, H Ar); 7.19–7.27 (2H, m, H Ar); 7.72 (1H, t, *J* = 7.6, H Ar); 7.85 (1H, t, *J* = 7.6, H Ar); 8.05 (1H, d, *J* = 8.0, H Ar); 8.21 (1H, d, *J* = 8.4, H Ar); 13.66 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.2; 71.3; 114.8; 115.7; 115.9; 121.2 (2C); 124.4 (2C); 124.5; 124.6; 126.2; 127.4; 129.0; 130.2; 142.1; 145.5; 145.7; 145.8; 150.3; 152.0; 152.7; 168.6. Found, %: C 69.73; H 4.34; N 4.29. $C_{18}H_{14}FNO_3$. Calculated, %: C 69.45; H 4.53; N 4.50.

**2-[(2-Chlorophenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7g)**. White solid. IR spectrum, ν, $cm^{-1}$: 3431 (COOH), 3019, 2964, 1726 (C=O), 1614, 1578, 1486. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.69 (3H, s, $CH_3$); 5.41 (2H, s, $ArCH_2O$); 6.84 (1H, t, *J* = 7.8, H Ar); 7.06 (1H, d, *J* = 8.4, H Ar); 7.12–7.15 (2H, m, H Ar); 7.72 (1H, t, *J* = 7.8, H Ar); 7.90 (1H, t, *J* = 8.4, H Ar); 8.08 (1H, d, *J* = 8.4, H Ar); 8.16 (1H, d, *J* = 7.8, H Ar); 13.61 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.2; 70.8; 111.6; 120.5; 125.4; 126.0; 126.5; 126.9; 127.8; 128.7; 128.9; 130.4; 131.9; 139.3; 147.2; 155.4; 156.7; 168.6. Found, %: C 65.75; H 4.50; N 4.05. $C_{18}H_{14}ClNO_3$. Calculated, %: C 65.96; H 4.31; N 4.27.

**2-[(4-Chlorophenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7h)**. White solid. IR spectrum, ν, $cm^{-1}$: 3431 (COOH), 3050, 2964, 1720 (C=O), 1602, 1573, 1486. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, $CH_3$); 5.37 (2H, s, $ArCH_2O$); 7.03 (2H, d, *J* = 8.8, H Ar); 7.34 (2H, d, *J* = 8.8, H Ar); 7.71 (1H, t, *J* = 7.6, H Ar); 7.84 (1H, t, *J* = 7.6, H Ar); 8.04 (1H, d, *J* = 8.4, H Ar); 8.20 (1H, d, *J* = 8.4, H Ar); 13.65 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.1; 70.9; 116.2; 124.5 (2C); 126.2; 127.3; 127.4; 128.9; 129.0; 130.2; 141.9; 145.4; 152.2; 156.7; 168.7. Found, %: C 66.32; H 4.52; N 4.05. $C_{18}H_{14}ClNO_3$. Calculated, %: C 65.96; H 4.31; N 4.27.

**2-[(2-Bromophenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7i)**. Pale-yellow solid. IR spectrum, ν, $cm^{-1}$: 3372 (COOH), 3067, 2855, 1724 (C=O), 1627, 1584, 1508. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.67 (3H, s, $CH_3$); 5.39 (2H, s, $ArCH_2O$); 6.84 (1H, t, *J* = 7.2, H Ar); 7.18 (1H, d, *J* = 7.6, H Ar); 7.26 (1H, t, *J* = 7.2, H Ar); 7.52 (1H, d, *J* = 7.6, H Ar); 7.67 (1H, t, *J* = 7.6, H Ar); 7.79 (1H, t, *J* = 7.6, H Ar); 8.00 (1H, d, *J* = 8.0, H Ar); 8.16 (1H, d, *J* = 7.6, H Ar); 13.57 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.2; 71.3; 110.8; 113.6; 122.1; 124.6; 126.3; 127.4; 127.5; 128.6; 129.1; 130.3; 132.8; 142.3; 145.5; 151.8; 154.2; 168.5. Found, %: C 57.95; H 3.54; N 3.94. $C_{18}H_{14}BrNO_3$. Calculated, %: C 58.08; H 3.79; N 3.76.

**2-[(4-Bromophenoxy)methyl]-4-methylquinoline-3-carboxylic acid (7j)**. Pale-yellow solid. IR spectrum, ν, $cm^{-1}$: 3445 (COOH), 3055, 2974, 1717 (C=O), 1601, 1571, 1488. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.72 (3H, s, $CH_3$); 5.39 (2H, s, $ArCH_2O$); 6.90 (2H, d, *J* = 8.4, H Ar); 7.08 (2H, d, *J* = 8.4, H Ar); 7.71 (1H, t, *J* = 7.8, H Ar); 7.90 (1H, t, *J* = 8.4, H Ar); 8.07 (1H, d, *J* = 8.4, H Ar); 8.17 (1H, d, *J* = 7.8, H Ar); 13.43 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.2; 70.6; 114.7; 125.1; 126.4; 127.7; 128.6; 128.9; 129.5; 129.8; 131.9; 139.5; 147.3; 155.4; 156.6; 168.5. Found, %: C 57.85; H 3.98; N 3.61. $C_{18}H_{14}BrNO_3$. Calculated, %: C 58.08; H 3.79; N 3.76.

**4-Methyl-2-[(naphthalen-1-yloxy)methyl]quinoline-3-carboxylic acid (7k)**. White solid. IR spectrum, ν, $cm^{-1}$: 3431 (COOH), 3065, 2931, 1718 (C=O), 1611, 1570, 1508. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, $CH_3$); 5.70 (2H, s, $ArCH_2O$); 7.58 (1H, t, *J* = 7.6, H Ar); 7.62–7.72 (4H, m, H Ar); 7.87 (1H, t, *J* = 7.2, H Ar); 7.94 (2H, t, *J* = 8.4, H Ar); 8.11 (1H, d, *J* = 8.0, H Ar); 8.23 (1H, d, *J* = 8.4, H Ar); 8.33 (1H, d, *J* = 8.4, H Ar); 13.64 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 14.8; 76.2; 120.1; 121.2; 122.8; 125.1; 125.2; 125.3; 126.5; 127.1; 127.3; 127.5; 129.1; 129.3; 130.9; 133.0; 136.2; 145.0; 146.6; 151.8; 156.9; 168.6. Found, %: C 77.20; H 4.82; N 3.93. $C_{22}H_{17}NO_3$. Calculated, %: C 76.95; H 4.99; N 4.08.

**4-Methyl-2-[(naphthalen-2-yloxy)methyl]quinoline-3-carboxylic acid (7l)**. White solid. IR spectrum, ν, $cm^{-1}$: 3438 (COOH), 3035, 2953, 1721 (C=O), 1603, 1569, 1509. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, $CH_3$); 5.48 (2H, s, $ArCH_2O$); 7.20 (1H, d, *J* = 8.8, H Ar); 7.35 (1H, t, *J* = 7.6, H Ar); 7.43 (1H, d, *J* = 7.6, H Ar); 7.47 (1H, s, H Ar); 7.70 (1H, t, *J* = 7.6, H Ar); 7.77 (1H, d, *J* = 8.4, H Ar); 7.82–7.85 (3H, m, H Ar); 8.06 (1H, d, *J* = 8.4, H Ar); 8.19 (1H, d, *J* = 8.0, H Ar); 13.74 (1H, s, COOH). $^{13}$C NMR spectrum, δ, ppm: 15.1; 70.5; 107.1; 118.4; 123.5; 124.5; 126.1; 126.3; 126.4; 127.2; 128.2; 128.4; 129.0 (2C); 130.0; 130.3; 133.8; 141.5; 145.4; 152.3; 155.8; 168.9. Found, %: C 76.82; H 4.68; N 4.29. $C_{22}H_{17}NO_3$. Calculated, %: C 76.95; H 4.99; N 4.08.

**Synthesis of 12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one derivatives 6a–j and 8-methylnaphthoxepino-[3,4-*b*]quinolin-7(14*H*)-ones 6k,l** (General method). The respective carboxylic acid **7a**–**l** (0.5 mmol) together with PPA (83% $P_2O_5$, 7.5 g) was added to a round-bottom flask (25 ml) and stirred at 145 °C for 4–6 h. The conversion was monitored by TLC. After the reaction was complete, the mixture was poured slowly with stirring into cold water followed by neutralization with saturated $NaHCO_3$ solution. The resulting precipitate was purified by flash chromatography (petroleum ether – EtOAc, 1:1). The yields and melting points are listed in Table 1.

**12-Methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6a)**. White needle crystals. IR spectrum, ν, $cm^{-1}$: 3059, 1706 (C=O), 1562, 1491, 1400, 1259, 1211, 1084, 1022, 871. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.67 (3H, s, $CH_3$); 5.35 (2H, s, H oxepine); 6.98 (1H, d, *J* = 8.0, H Ar); 7.04 (1H, t, *J* = 7.6, H Ar); 7.41 (1H, td, *J* = 8.4, *J* = 1.2, H Ar); 7.54 (1H, t, *J* = 8.0, H Ar); 7.70 (1H, t, *J* = 7.6, H Ar); 7.94 (1H, dd, *J* = 8.0, *J* = 1.2, H Ar); 8.01–8.06 (2H, m, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.2; 75.7; 120.2; 122.0; 125.0; 127.3; 127.7; 130.0; 130.7; 130.8; 131.0; 134.9; 135.4; 145.6; 147.4; 152.2; 160.0; 193.9. Found, %: C 78.82; H 4.56; N 4.98. $C_{18}H_{13}NO_2$. Calculated, %: C 78.53; H 4.76; N 5.09.

**4,12-Dimethyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6b)**. White needle crystals. IR spectrum, ν, $cm^{-1}$: 3065, 2961, 2864, 1710 (C=O), 1592, 1510, 1447, 1395, 1262, 1208, 1176, 1068, 865. $^1$H NMR spectrum, δ, ppm

(*J*, Hz): 2.19 (3H, s, $CH_3$); 2.66 (3H, s, $CH_3$); 5.38 (2H, s, H oxepine); 6.94 (1H, t, *J* = 7.6, H Ar); 7.28 (1H, d, *J* = 7.2, H Ar); 7.54 (1H, t, *J* = 8.0, H Ar); 7.70 (1H, t, *J* = 7.6, H Ar); 7.79 (1H, d, *J* = 8.0, H Ar); 8.02–8.06 (2H, m, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.5; 16.6; 75.6; 121.4; 124.9; 126.4; 127.2; 128.8; 130.0; 130.6; 130.9; 133.7; 135.9; 136.4; 145.4; 147.4; 152.3; 158.2; 194.3. Found, %: C 78.65; H 5.16; N 5.16. $C_{19}H_{15}NO_2$. Calculated, %: C 78.87; H 5.23; N 4.84.

**4-Methoxy-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6c)**. White solid. IR spectrum, ν, cm$^{-1}$: 3047, 2966, 2818, 1699, 1613, 1592, 1517, 1457, 1410, 1387, 1298, 1235, 1147, 1081, 851. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, $CH_3$); 3.83 (3H, s, $OCH_3$); 5.48 (2H, s, H oxepine); 7.14 (1H, d, *J* = 8.0, H Ar); 7.30 (1H, d, *J* = 7.6, H Ar); 7.51 (1H, t, *J* = 7.6, H Ar); 7.75 (1H, t, *J* = 7.6, H Ar); 7.90 (1H, t, *J* = 7.6, H Ar); 8.13 (1H, d, *J* = 8.4, H Ar); 8.26 (1H, d, *J* = 8.4, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.4; 56.5; 75.9; 117.2; 121.7; 121.9; 126.0; 127.2; 127.7; 128.2; 129.9; 131.7; 133.5; 145.3; 147.3; 149.9; 150.3; 152.5; 193.2. Found, %: C 74.40; H 5.25; N 4.22. $C_{19}H_{15}NO_3$. Calculated, %: C 74.74; H 4.95; N 4.59.

**3-Methoxy-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6d)**. White needle crystals. IR spectrum, ν, cm$^{-1}$: 3039, 2972, 2867, 1710, 1608, 1593, 1523, 1474, 1411, 1359, 1226, 1168, 1035, 852. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.74 (3H, s, $CH_3$); 3.86 (3H, s, $OCH_3$); 5.46 (2H, s, H oxepine); 6.66 (1H, d, *J* = 2.4, H Ar); 6.83 (1H, dd, *J* = 8.4, *J* = 2.4, H Ar); 7.77 (1H, t, *J* = 8.4, H Ar); 7.92 (1H, t, *J* = 8.4, H Ar); 7.95 (1H, d, *J* = 8.4, H Ar); 8.13 (1H, d, *J* = 8.0, H Ar); 8.30 (1H, d, *J* = 8.4, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.6; 56.3; 76.1; 103.2; 110.7; 120.3; 126.0; 127.8; 128.2; 129.8; 131.6; 132.9; 133.4; 145.9; 147.1; 152.8; 161.9; 165.4; 191.2. Found, %: C 75.54; H 4.89; N 4.72. $C_{19}H_{15}NO_3$. Calculated, %: C 74.74; H 4.95; N 4.59.

**2-Methoxy-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6e)**. White needle crystals. IR spectrum, ν, cm$^{-1}$: 3046, 2978, 2890, 1707, 1613, 1588, 1527, 1496, 1406, 1363, 1247, 1190, 1024, 846. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.82 (3H, s, $CH_3$); 3.92 (3H, s, $OCH_3$); 5.44 (2H, s, H oxepine); 7.05 (1H, d, *J* = 8.8, H Ar); 7.16 (1H, dd, *J* = 8.8, *J* = 3.2, H Ar); 7.54 (1H, t, *J* = 3.2, H Ar); 7.69 (1H, t, *J* = 8.0, H Ar); 7.84 (1H, t, *J* = 8.0, H Ar); 8.17 (1H, d, *J* = 8.4, H Ar); 8.19 (1H, d, *J* = 8.4, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.5; 55.9; 76.0; 111.8; 121.4; 123.9; 125.0; 126.2; 127.5; 128.0; 129.9; 130.9; 133.2; 146.0; 147.3; 152.5; 154.3; 154.8; 193.4. Found, %: C 74.96; H 5.07; N 4.51. $C_{19}H_{15}NO_3$. Calculated, %: C 74.74; H 4.95; N 4.59.

**4-Fluoro-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6f)**. White solid. IR spectrum, ν, cm$^{-1}$: 3059, 2967, 2885, 1707, 1622, 1594, 1534, 1498, 1401, 1378, 1256, 1185, 1036, 872. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.71 (3H, s, $CH_3$); 5.57 (2H, s, H oxepine); 7.17–7.22 (1H, m, H Ar); 7.60 (1H, t, *J* = 8.4, H Ar); 7.74–7.78 (2H, m, H Ar); 7.91 (1H, t, *J* = 7.6, H Ar); 8.12 (1H, d, *J* = 8.4, H Ar); 8.27 (1H, d, *J* = 8.4, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.6; 76.3; 121.3; 121.5; 121.9; 122.2; 122.3; 126.1 (2C); 127.6; 127.8; 128.5; 128.7; 129.9; 131.7; 133.2; 133.3; 146.1; 147.3; 151.4; 152.1; 153.8; 192.3. Found, %: C 73.92; H 4.19; N 4.62. $C_{18}H_{12}FNO_2$. Calculated, %: C 73.71; H 4.12; N 4.78.

**4-Chloro-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6g)**. Pale-yellow needle crystals. IR spectrum, ν, cm$^{-1}$: 3062, 2991, 2875, 1697, 1611, 1588, 1507, 1488, 1414, 1377, 1297, 1164, 1042, 869. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.74 (3H, s, $CH_3$); 5.47 (2H, s, H oxepine); 6.99 (1H, t, *J* = 7.6, H Ar); 7.53 (1H, d, *J* = 7.2, H Ar); 7.58 (1H, t, *J* = 7.2, H Ar); 7.73 (1H, t, *J* = 7.2, H Ar); 7.87 (1H, d, *J* = 7.6, H Ar); 8.04–8.08 (2H, m, H Ar). $^{13}$C NMR spectrum, δ, ppm: 14.3; 75.2; 120.8; 123.7; 124.0; 126.7; 126.8; 126.9; 128.6; 129.1; 130.1; 132.2; 134.4; 144.8; 146.5; 150.5; 154.4; 191.9. Found, %: C 69.45; H 4.15; N 4.20. $C_{18}H_{12}ClNO_2$. Calculated, %: C 69.80; H 3.90; N 4.52.

**2-Chloro-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6h)**. Yellow solid. IR spectrum, ν, cm$^{-1}$: 3050, 2978, 1707, 1617, 1595, 1489, 1402, 1368, 1256, 1126, 1027, 981. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.32 (3H, s, $CH_3$); 5.93 (2H, s, H oxepine); 7.35 (1H, d, *J* = 8.0, H Ar); 7.79 (1H, d, *J* = 7.6, H Ar); 8.27–8.33 (2H, m, H Ar); 8.49–8.53 (2H, m, H Ar); 8.78 (1H, d, *J* = 8.0, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.6; 75.8; 120.1; 121.9; 127.4; 128.3; 128.4; 128.5; 128.6; 129.2; 132.3; 136.8; 140.0; 148.3; 148.9; 151.6; 157.5; 192.8. Found, %: C 69.52; H 4.01; N 4.23. $C_{18}H_{12}ClNO_2$. Calculated, %: C 69.80; H 3.90; N 4.52.

**4-Bromo-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6i)**. Yellow solid. IR spectrum, ν, cm$^{-1}$: 3048, 1710, 1613, 1597, 1559, 1478, 1398, 1306, 1279, 1177, 1047, 910. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.67 (3H, s, $CH_3$); 5.46 (2H, s, H oxepine); 6.93 (1H, t, *J* = 8.0, H Ar); 7.57 (1H, t, *J* = 7.6, H Ar); 7.70 (1H, d, *J* = 8.0, H Ar); 7.74 (1H, d, *J* = 7.6, H Ar); 7.91 (1H, d, *J* = 8.4, H Ar); 8.03–8.08 (2H, m, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.6; 76.1; 114.0; 122.3; 122.6; 124.9; 125.0; 127.5; 127.9; 130.0; 130.6; 131.3; 138.6; 145.9; 147.4; 151.5; 156.2; 192.8. Found, %: C 60.75; H 3.19; N 3.74. $C_{18}H_{12}BrNO_2$. Calculated, %: C 61.04; H 3.41; N 3.95.

**2-Bromo-12-methyl[1]benzoxepino[3,4-*b*]quinolin-13(6*H*)-one (6j)**. Yellow solid. IR spectrum, ν, cm$^{-1}$: 3046, 2989, 2876, 1705, 1578, 1519, 1488, 1397, 1310, 1230, 1177, 1047, 939. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.75 (3H, s, $CH_3$); 5.41 (2H, s, H oxepine); 6.95 (1H, d, *J* = 8.8, H Ar); 7.55 (1H, dd, *J* = 8.4, *J* = 2.4, H Ar); 7.65 (1H, t, *J* = 7.6, H Ar); 7.80 (1H, t, *J* = 8.0, H Ar); 8.11–8.14 (3H, m, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.5; 75.8; 110.0; 114.4; 122.1; 125.1; 127.7; 127.8; 128.0; 129.9; 131.2; 133.1; 137.8; 146.4; 147.4; 151.7; 159.0; 192.3. Found, %: C 61.21; H 3.27; N 4.18. $C_{18}H_{12}BrNO_2$. Calculated, %: C 61.04; H 3.41; N 3.95.

**8-Methylnaphtho[2',1':6,7]oxepino[3,4-*b*]quinolin-7(14*H*)-one (6k)**. White solid. IR spectrum, ν, cm$^{-1}$: 3043, 2986, 1691, 1604, 1580, 1527, 1480, 1397, 1308, 1238, 1191, 1051, 906. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, $CH_3$); 5.59 (2H, s, H oxepine); 7.41–7.45 (2H, m, H Ar); 7.51 (1H, d, *J* = 7.6, H Ar); 7.55 (1H, t, *J* = 7.6, H Ar); 7.71 (2H, t, *J* = 8.0, H Ar); 7.97 (1H, d, *J* = 8.8,

H Ar); 8.04 (1H, d, *J* = 8.4, H Ar); 8.08 (1H, d, *J* = 8.4, H Ar); 8.33 (1H, d, *J* = 8.4, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.9; 76.0; 120.7; 121.0; 122.2; 122.6; 123.7; 124.9; 125.1; 125.8; 126.1; 127.0; 127.8; 128.1; 128.8; 130.0; 130.5; 131.3; 136.9; 152.0; 158.1; 193.6. Found, %: C 80.90; H 4.71; N 4.01. $C_{22}H_{15}NO_2$. Calculated, %: C 81.21; H 4.65; N 4.30.

**14-Methylnaphtho[1',2':6,7]oxepino[3,4-*b*]quinolin-15(8*H*)-one (6l)**. White solid. IR spectrum, ν, cm$^{-1}$: 3056, 1688, 1593, 1507, 1486, 1434, 1397, 1322, 1274, 1218, 1191, 1123, 1051, 906. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.83 (3H, s, $CH_3$); 5.63 (2H, s, H oxepine); 7.22 (1H, d, *J* = 8.8, H Ar); 7.53 (1H, t, *J* = 8.0, H Ar); 7.68 (1H, t, *J* = 7.6, H Ar); 7.72 (1H, t, *J* = 8.0, H Ar); 7.83 (1H, t, *J* = 8.0, H Ar); 7.86 (1H, d, *J* = 7.6, H Ar); 7.95 (1H, d, *J* = 8.8, H Ar); 8.13 (1H, d, *J* = 8.0, H Ar); 8.21 (1H, d, *J* = 8.4, H Ar); 8.95 (1H, d, *J* = 8.8, H Ar). $^{13}$C NMR spectrum, δ, ppm: 15.0; 74.2; 118.8; 120.7; 124.3; 124.6; 124.8; 127.5; 128.0; 128.6; 128.9; 129.5; 129.8; 130.6; 130.9; 135.4; 136.4; 142.9; 147.0; 150.5; 159.1; 197.6. Found, %: C 81.44; H 4.90; N 4.15. $C_{22}H_{15}NO_2$. Calculated, %: C 81.21; H 4.65; N 4.30.

Supplementary information file containing the $^1$H and $^{13}$C NMR spectra of compounds **7a**–**l** and **6a**–**l** is available at the journal website at http://link.springer.com/journal/10593.

*The project was financially supported by the National Natural Science Foundation of China (Nos. 21476028 and 21402011) and the Natural Science Foundation of Liaoning Province (No. 201602006).*

## References


1. Huang, S. T.; Kuo, H. S.; Chen, C. T. *Tetrahedron Lett.* **2001**, *42*, 7473.
2. Bruder, M.; Haseler, P. L.; Muscarella, M.; Lewis, W.; Moody, C. J. *J. Org. Chem.* **2010**, *75*, 353.
3. Pettit, G. R.; Numata, A.; Iwamoto, C.; Usami, Y.; Yamada, T.; Ohishi, H.; Cragg, G. M. *J. Nat. Prod.* **2006**, *69*, 323.
4. Boonphong, S.; Puangsombat, P.; Baramee, A.; Mahidol, C.; Ruchirawat, S.; Kittakoop, P. *J. Nat. Prod.* **2007**, *70*, 795.
5. Sarkhel, S.; Sharon, A.; Trivedi, V.; Maulik, P. R.; Singh, M. M.; Venugopalan, P.; Ray, S. *Bioorg. Med. Chem.* **2003**, *11*, 5025.
6. Saidachary, G.; Prasad, K. V.; Divya, D.; Singh, A.; Ramesh, U.; Sridhar, B.; Raju, B. C. *Eur. J. Med. Chem.* **2014**, *76*, 460.
7. Kahnberg, P.; Sterner, O. *Tetrahedron* **2001**, *57*, 7181.
8. Lee, S. H.; Van, H. T. M.; Yang, S. H.; Lee, K. T.; Kwon, Y.; Cho, W. J. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2444.
9. Liu, J. H.; Steigel, A.; Reininger, E.; Bauer, R. *J. Nat. Prod.* **2000**, *63*, 403.
10. Staben, S. T.; Siu, M.; Goldsmith, R.; Olivero, A. G.; Do, S.; Burdick, D. J.; Heffron, T. P.; Dotson, J.; Sutherlin, D. P.; Zhu, B. Y.; Tsui, V.; Le, H.; Lee, L.; Lesnick, J.; Lewis, C.; Murray, J. M.; Nonomiya, J.; Pang, J.; Prior, W. W.; Salphati, L.; Rouge, L.; Sampath, D.; Sideris, S.; Wiesmann, C.; Wu, P. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 4054.
11. Kamboj, R. C.; Jindal, P.; Kumar, D.; Khullar, S.; Mandal, S. K. *J. Photochem. Photobiol. A: Chem.* **2014**, *278*, 31.
12. Rao Mangina, N. S. V. M.; Suresh, S.; Sridhar, B.; Karunakar, G. V. *Org. Biomol. Chem.* **2016**, *14*, 3526.
13. Rao Mangina, N. S. V. M.; Kadiyala, V.; Guduru, R.; Goutham, K.; Sridhar, B.; Karunakar, G. V. *Org. Lett.* **2017**, *19*, 282.
14. Johnson, O. H.; Hamilton, C. S. *J. Am. Chem. Soc.* **1941**, *63*, 2864.
15. LaMontagne, M. P.; Dagli, D.; Khan, M. S.; Blumbergs, P. *J. Med. Chem.* **1980**, *23*, 981.
16. Urbina, J. M.; Cortés, J. C. G.; Palma, A.; López, S. N.; Zacchino, S. A.; Enriz, R. D.; Ribas, J. C.; Kouznetzov, V. V. *Bioorg. Med. Chem.* **2000**, *8*, 691.
17. Jain, R.; Vaitilingam, B.; Nayyar, A.; Palde, P. B. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1051.
18. Ulven, T.; Little, P. B.; Receveur, J. M.; Frimurer, T. M.; Rist, Ø.; Nørregaard, P. K.; Högberg, T. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1070.
19. Li, A.; Huang, C.; Luo, C. W.; Li, L. J.; Yi, W. J.; Liu, T. W.; Chao, Z. S. *Catal. Commun.* **2017**, *98*, 13.
20. Dolle, R. E.; Nelson, K. H. *J. Comb. Chem.* **1999**, *1*, 235.
21. Gao, W. T.; Lin, G. H.; Li, Y.; Tao, X. Y.; Liu, R.; Sun, L. J. *Beilstein J. Org. Chem.* **2012**, *8*, 1849.
22. Gao, W. T.; Xing, X. D.; Li, Y.; Lan, S. *Tetrahedron* **2014**, *70*, 2180.
23. Gao, W. T.; Fu, X. B.; Zhang, X. F.; Zhao, Y. N.; Wang, D. F.; Li, Y. *Tetrahedron Lett.* **2016**, *57*, 4145.
24. Li, Y.; Li, K.; Gao, W. T. *Chem. Heterocycl. Compd.* **2016**, *52*, 200. [*Khim. Geterotsikl. Soedin.* **2016**, *52*, 200.]
25. Li, Y.; Wang, Y.; Zou, H. T. *Mol. Diversity* **2017**, *21*, 463.
26. Jida, M.; Deprez, B. *New J. Chem.* **2012**, *36*, 869.
27. Ryabukhin, S. V.; Volochnyuk, D. M.; Plaskon, A. S.; Naumchik, V. S.; Tolmachev, A. A. *Synthesis* **2007**, 1214.
28. Degtyarenko, A. S.; Tolmachev, A. A.; Volovenko, Y. M.; Tverdokhlebov, A. V. *Synthesis* **2007**, 3891.
29. Xu, J.; Wang, D. L.; Liu, Z. P.; Zhang, K. X.; Ma, W.; Liu, B. *Heterocycles* **2017**, *94*, 1055.
30. Nammalwar, B.; Murie, M.; Fortenberry, C.; Bunce, R. A. *Tetrahedron Lett.* **2014**, *55*, 3181.
31. Eaton, P. E.; Carlson, G. R.; Lee, J. T. *J. Org. Chem.* **1973**, *38*, 4071.
32. Meesala, R.; Nagarajan, R. *Tetrahedron Lett.* **2010**, *51*, 422.