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Base-Promoted Formal [4 + 3] Annulation between 2-Fluorophenylacetylenes and Ketones: A Route to Benzoxepines

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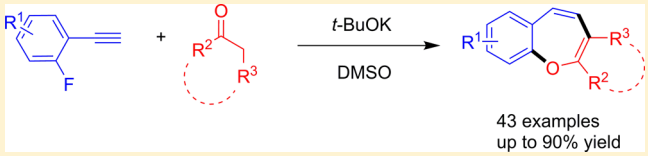
Supporting Information

ABSTRACT: The first base-promoted formal [4 + 3] annulation between 2-fluorophenylacetylenes and ketones has been disclosed. The reaction proceeds through a tandem α-vinylation of ketones followed by an intramolecular nucleophilic aromatic substitution (S_NAr) reaction of the *in situ* generated β,γ-unsaturated ketone intermediates, providing a straightforward access to a wide range of functionalized benzoxepines in moderate to high yields. The transition-metal-free methodology featured a wide substrate scope, the use of easily available starting materials, and a high functional group tolerance.



INTRODUCTION

Benzoxepines are an important class of seven-membered oxygen-containing heterocycles widely distributed in a variety of natural products and biologically active compounds,[1] such as pterulinic acid,[1a] ptaeroxylin,[1b] and artoristilbene[1c] (Figure 1). Interestingly, some of the benzoxepine derivatives isolated from sunflower can serve as natural herbicides.[2] Therefore, the development of facile and efficient strategies for the straightforward construction of these important ring systems with simple and readily available starting materials is of great significance.[3]

In the past decades, many elegant transition-metal-catalyzed intramolecular cyclization reactions have been developed for the synthesis of functionalized benzoxepines,[1d,4] such as osmium-catalyzed 7-endo heterocyclization of aromatic alkynols,[4a] Rh-catalyzed intramolecular olefin hydroacylation,[4c] and gold-catalyzed tandem intramolecular cyclization of 2-(prop-2-ynyloxy)benzaldehydes.[4f] On the other hand, transition-metal-catalyzed intermolecular [m + n] cyclization has also proven to be a powerful tool for the assembly of these ring structures.[5] For example, Lu and co-workers reported cationic palladium-catalyzed [5 + 2] annulations of 2-aroylmethoxyarylboronic acids with alkynes or allenoates.[5b,c] Zhang et al. developed a copper-catalyzed tandem [4 + 3] cyclization reaction of trifluoromethyl-containing *ortho*-halo-β-chlorostyrenes with ketones for the synthesis of a variety of 4-trifluoromethyl-benzoxepines (Figure 2a).[5d] Most recently, Mascareñ and Gulías reported a rhodium-catalyzed formal [5 + 2] cycloaddition of *o*-vinylphenols with alkynes, giving rise to the corresponding benzoxepines (Figure 2b).[6] In contrast, transition-metal-free synthetic strategies for preparing these seven-membered heterocyclic compounds have been less explored.[7] Thus, the development of general methods for constructing benzoxepine derivatives with a wide substrate scope under transition-metal-free conditions is highly appealing.[8]

As part of our continuing interest in the development of efficient methods for the synthesis of oxygen and/or nitrogen containing heterocyclic compounds,[9] herein, we wish to report a convenient method for the synthesis of benzoxepines via a base-promoted [4 + 3] cyclization of readily available ketones and 2-fluorophenylacetylenes (Figure 2c).

RESULTS AND DISCUSSION

Our initial efforts focused on the reaction of 2-fluorophenylacetylene (**1a**) and acetophenone (**2a**) under various reaction conditions, and the results are summarized in Table 1. To our delight, when the reaction was performed in the presence of 1 equiv of *t*-BuOK in DMSO at 120 °C for 12 h, the desired product **3aa**, 2-phenylbenzo[*b*]oxepine, was obtained in 92% yield (entry 1). Further screening of bases showed that CH_3ONa, KOH, and DBU were also capable of promoting the reaction to give the desired product in good yields while replacement of *t*-BuOK by other organic or inorganic bases such as K_2CO_3, Et_3N, or *t*-BuOLi led to low yields (entries 2−8). Decreasing the loading of *t*-BuOK to 0.5 equiv decreased the yield to 45% (entry 9). It should be pointed out that the reaction required a nitrogen atmosphere to proceed; if the reaction was conducted in air, the product was obtained only in 9% yield along with a large amount of unidentified products (entry 10). It was also found that the solvent have a great influence on the yield of **3aa**. DMSO proved to be the most suitable media for the reaction while other solvents such as DMF, MeCN, 1,4-dioxane, or toluene retarded the formation of **3aa** (entries 11−14). Further optimization revealed that decreasing the reaction temperature from 120 to 100 °C led to an obvious decrease in the yield of the product (entry 15).

With the optimized reaction conditions in hand, the base-promoted methodology was first applied for the reactions of

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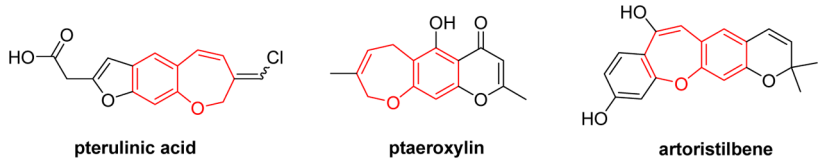


Figure 1. Representative natural products containing the benzoxepine skeleton.

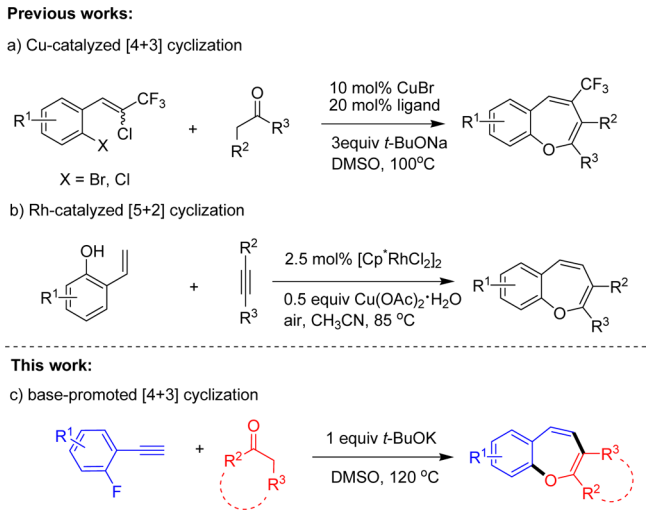
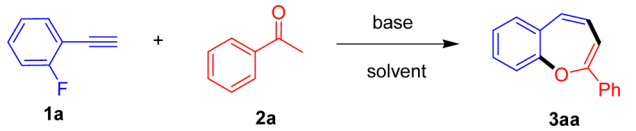


Figure 2. Synthetic strategies to benzoxepines.

Table 1. Optimization of the Reaction Conditions[a]



entry	base	solvent	temp (°C)	yield (%)[b]
1	*t*-BuOK	DMSO	120	92 (86)
2	CH_3ONa	DMSO	120	81
3	C_2H_5ONa	DMSO	120	43
4	K_2CO_3	DMSO	120	68
5	KOH	DMSO	120	88
6	DBU	DMSO	120	75
7	Et_3N	DMSO	120	30
8	*t*-BuOLi	DMSO	120	25
9[c]	*t*-BuOK	DMSO	120	45
10[d]	*t*-BuOK	DMSO	120	9
11	*t*-BuOK	DMF	120	18
12	*t*-BuOK	MeCN	120	trace
13	*t*-BuOK	1,4-dioxane	120	15
14	*t*-BuOK	toluene	120	trace
15	*t*-BuOK	DMSO	100	79

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.25 mmol), and base (0.25 mmol) in solvent (1 mL), under a N_2 atmosphere for 12 h. [b]GC yield with dodecane as internal standard. Number in parentheses is the yield of isolated product. [c]With 0.5 equiv of *t*-BuOK. [d]The reaction was conducted in air.

2-fluorophenylacetylene (**1a**) with various ketones. As can be seen from Table 2, the cyclization is efficient for a wide range of alkyl aromatic, alkyl heteroaromatic, aliphatic, and cycloaliphatic ketones. A variety of acetophenones worked well with **1a** to give the corresponding products in good yields. Both electron-donating and -withdrawing groups such as the methyl, trifluoromethyl, dimethylamino, and morpholino group were tolerated (**3ab**−**3ac**) without any difficulty under the reaction conditions. In addition to monosubstituted acetophenones, bis-substituted acetophenone **2e** provided the desired product **3ae** in high yield as well. Remarkably, methyl ketones containing a naphthyl, furan, or thiophene moiety are all suitable substrates for this transformation (**3af**−**3ag**). As expected, other aromatic ketones such as propiophenones and deoxybenzoins with different substitution patterns reacted well with **1a** to form the corresponding benzoxepines **3ah** and **3ai** in good yields. It should be pointed out that 1,4-diacetylbenzene failed to react with 2-fluorophenylacetylene to yield the desired product under the standard reaction conditions, and a large amount of starting material was recovered, although the reason is unclear.

Pleasingly, a range of alkyl benzyl ketones underwent the cyclization smoothly to afford the desired products in moderate to high yields (**3aj**−**3ao**). The results show that the electronic nature of the substituents on the benzene ring affects the yields of the desired products slightly. However, steric hindrance has a great impact on the reaction. For instance, only 54% yield was obtained when (2-methoxyphenyl)acetone reacted with **1a** while its 4- and 3-substituted analogues gave higher yields (83% and 72%, respectively). (2-Furyl)acetone and (2-pyridyl)-acetone successfully entered into the reaction to furnish the corresponding products (**3ap** and **3aq**) in satisfactory yields. Note that the *β*-aryl-substituted aliphatic ketone, 4-phenylbutan-2-one (**2r**), could afford the product **3ar** in good yield with excellent regioselectivity (13:1). Both 3-pentanone and 1-cyclopropylethanone were capable of taking part in the process, although the latter gave the desired product in a lower yield (54%). Encouraged by these results, we further examined the scope of our new protocol with a series of cycloaliphatic ketones. To our delight, all three substrates examined, i.e., cyclohexanone, cycloheptanone, and cyclooctanone, underwent a smooth reaction with **1a**, affording the corresponding tricyclic products (**3au**−**3aw**) in good yields. To our surprise, the reaction of 2-tetralone led to an unexpected outcome. A tetracyclic compound, 12,13-dihydrobenzo[*b*]naphtho[1,2-*f*]-oxepine (**3ax**), was isolated in 82% yield, instead of the expected product **3ax′** (Scheme 1). It seems that **3ax** was formed through the aromatization of intermediate **3ax′**, which might be attributed to the higher thermodynamical stability of **3ax** than that of **3ax′**. The structures of the products **3ai**$_3$ and **3ax** were confirmed unambiguously by X-ray crystallography (Figure S1).[10]

Subsequently, the scope of 2-fluorophenylacetylenes was examined (Table 3). To our delight, a variety of electron-donating and -withdrawing substituents in the benzene ring of the 2-fluorophenylacetylenes, including halide (Cl, Br), CN, and methyl, are tolerated in this transformation, and the corresponding products (**3ba**−**3fa** and **3bj**$_2$−**3dj**$_2$) are obtained in high to excellent yields. Moreover, 3-ethynyl-2-fluoropyridine (**1g**) could undergo the annulation reaction with acetophenone (**2a**) to give rise to the corresponding product 2-phenyl-oxepino[2,3-*b*]pyridine (**3ga**) in a moderate yield.

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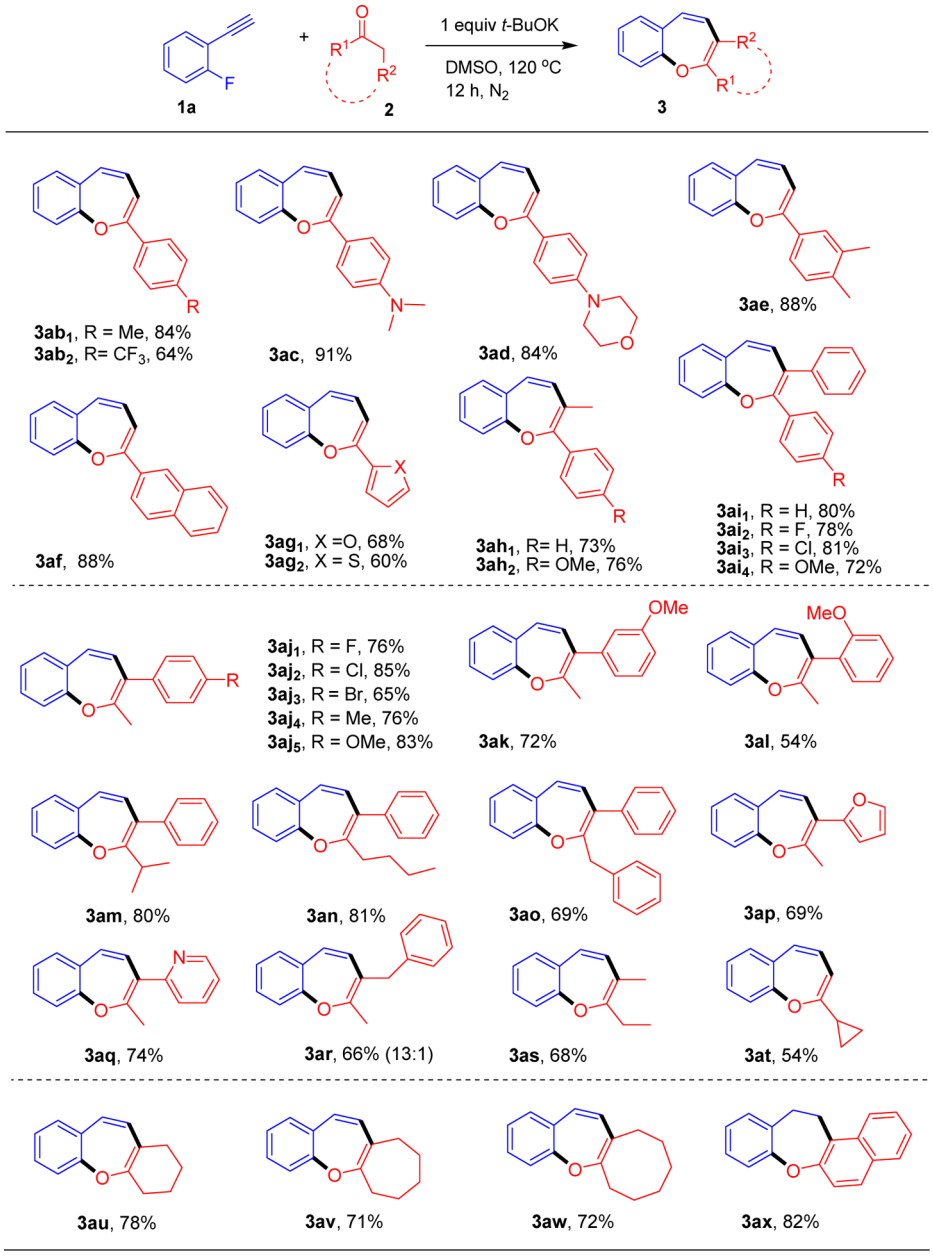
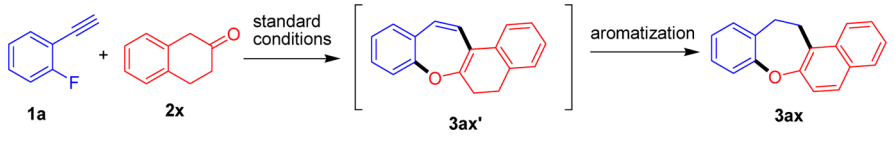
Table 2. Substrate Scope of Ketones[a,b]



[a]Reaction conditions: 2-fluorophenylacetylene (**1a**, 0.25 mmol), ketone **2** (0.25 mmol), and *t*-BuOK (0.25 mmol), in DMSO (1 mL) at 120 °C under a N_2 atmosphere for 12 h. [b]Isolated yields.

Scheme 1. Formation of 3ax through the Aromatization of 3ax′



In order to further demonstrate the practicability and reliability of the developed protocol, we also performed the reaction on a larger scale. Pleasingly, benzoxepine product **3aa** could be obtained in a satisfactory yield (75%) when the reaction was conducted on a 5 mmol scale (Scheme 2).

To obtain more insights into the mechanism of this transformation, we attempted to identify the reaction intermediates. Fortunately, when the reaction of 2-fluorophenylacetylene (**1a**) and 1-(furan-2-yl)ethanone (**2g$_1$**) was interrupted after 1 h, a *β*,*γ*-unsaturated ketone product **4ag$_1$** was observed in 48% yield by means of GC-MS analysis (eq 1). After purification and subsequent treatment with *t*-BuOK under standard conditions, **4ag$_1$** was able to give the product **3ag$_1$** in a 78% yield (eq 2), indicating that **4ag$_1$** might be the key intermediate for the formation of **3ag$_1$** and that the C−C bond formation would occur prior to the formation of C−O bond during the

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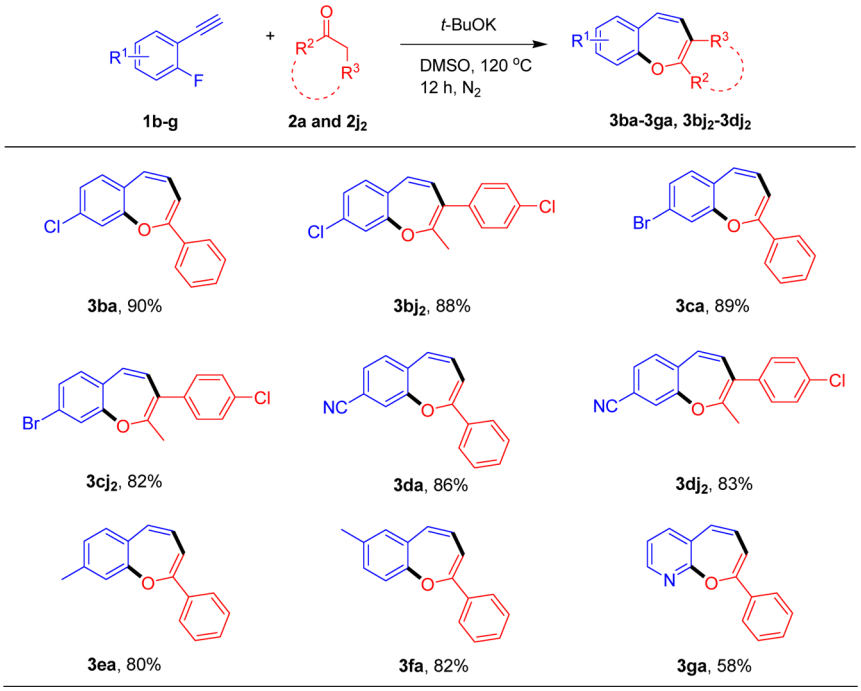
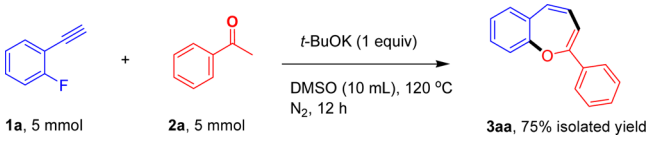
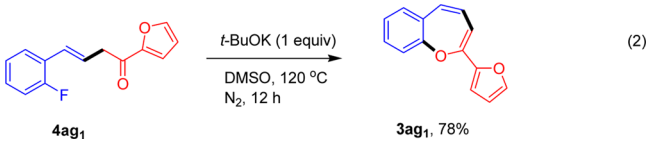
Table 3. Substrate Scope of 2-Fluorophenylacetylenes[a,b]

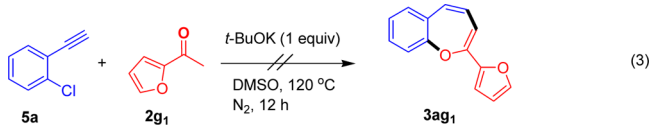


[a]Reaction conditions: alkyne **1** (0.25 mmol), ketone **2** (0.25 mmol), and *t*-BuOK (0.25 mmol), in DMSO (1 mL) at 120 °C under a N_2 atmosphere for 12 h. [b]Isolated yields.

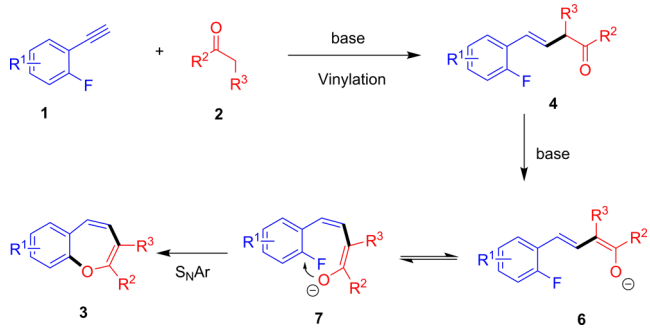
Scheme 2. Synthesis of 3aa on a Larger Scale







Scheme 3. Proposed Reaction Mechanism



cyclization process. Moreover, when 2-chlorophenylacetylene (**5a**) was employed to react with $\mathbf{2g_1}$ under standard conditions, only a complex mixture was observed without the formation of the desired product (eq 3), suggesting that the presence of a fluorine atom in the position ortho to the acetylenic group in molecules **1** is crucial to the success of the transformation.

On the basis of the above results and previous literature,[11,12] a plausible mechanism is illustrated in Scheme 3. Initially, vinylation of ketone **2** with *ortho*-fluorophenylacetylene **1** would take place in the presence of a base, giving rise to intermediate **4**.[11] The keto−enol tautomerism of **4** then occurred to yield an intermediate **6**, which was in equilibrium with its (*Z*)-isomer **7**. Finally, intramolecular nucleophilic aromatic substitution (S_NAr) of **7** would afford the target product **3**.[12]

CONCLUSION

In summary, we have successfully developed a facile and efficient protocol for the straightforward assembly of a wide range of functionalized benzoxepines via a base-promoted formal [4 + 3] annulation between 2-fluorophenylacetylenes and ketones. The reaction was proposed to proceed through a tandem α-vinylation of ketones followed by an intramolecular nucleophilic aromatic substitution (S_NAr) reaction. The transition-metal-free methodology featured a wide substrate scope, the

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use of easily available starting materials, and a high functional group tolerance. Further investigations into the mechanism and application of the method for constructing more complex molecules are ongoing in our laboratory.

EXPERIMENTAL SECTION

General Methods. ^{1}H and ^{13}C NMR spectra were recorded by using a 400 MHz NMR spectrometer. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively, and $CDCl_3$ is used as a solvent with TMS as the internal standard. Mass spectra were recorded on a gas chromatograph−mass spectrometer. The data of HRMS were collected using a high-resolution mass spectrometer (LCMS-IT-TOF). IR spectra were obtained using either potassium bromide plates or liquid films between two potassium bromide plates with an infrared spectrometer. Melting points were determined with a digital melting point measuring instrument. Compounds **1b−g** were synthesized according to the literature procedures.[13] Other substrates were commercially purchased and used without further purification.

General Procedure for the Preparation of Benzoxepines (3). To a 25 mL dried Schlenk tube was added the mixture of *o*-fluorophenylacetylene **1** (0.25 mmol), ketone **2** (0.25 mmol), and potassium *tert*-butoxide (0.25 mmol) in DMSO (1.0 mL) successively. The mixture was stirred at 120 °C for 12 h under a N_2 atmosphere. After the reaction was completed, the mixture was cooled to room temperature and diluted with H_2O (15 mL), neutralized with NH_4Cl, and extracted with EtOAc (10 mL × 3). The organic extract was washed with H_2O (10 mL × 3) and dried over anhydrous Mg_2SO_4. After removal of the EtOAc in vacuum, the crude product thus obtained was purified by column chromatography on silica gel with hexanes or petroleum ether/ethyl acetate (2:1 to 50:1) to give the desired products **3**.

*2-Phenylbenzo[b]oxepine (**3aa**).*[14] Yellow solid (47.3 mg, 86%), mp: 59−60 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.0 Hz, 2 H), 7.41 (t, J = 7.5 Hz, 2 H), 7.37−7.28 (m, 2 H), 7.19 (d, J = 7.4 Hz, 1 H), 7.12 (dd, J = 14.8, 7.6 Hz, 2 H), 6.80 (d, J = 10.0 Hz, 1 H), 6.32−6.28 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 154.9, 134.8, 132.1, 131.5, 130.3, 128.8, 128.6, 128.5, 127.5, 125.4, 124.8, 121.3, 110.1. IR (KBr): 3060, 3024, 2923, 2851, 1589, 1486, 1447, 1202, 1170, 752, 717, 687 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{16}H_{12}NaO$ $[M + Na]^+$: 243.0780; found: 243.0775.

*2-(p-Tolyl)benzo[b]oxepine (**3ab$_1$**).* Yellow solid (49.1 mg, 84%), mp: 81−82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.6 Hz, 2 H), 7.31 (t, J = 7.6 Hz, 1 H), 7.24−7.19 (m, 3 H), 7.13 (dd, J = 15.2, 7.6 Hz, 2 H), 6.79 (d, J = 10.8 Hz, 1 H), 6.34−6.29 (m, 1 H), 6.25 (d, J = 6.0 Hz, 1 H), 2.40 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 155.0, 138.6, 132.1(4), 132.1(0), 131.0, 130.2, 129.2, 128.7, 127.6, 125.4, 124.7, 121.3, 109.2, 21.2. IR (KBr): 3062, 3025, 2920, 2856, 1633, 1588, 1484, 1449, 1264, 1203, 1171, 1047, 776, 754 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{14}NaO$ $[M + Na]^+$: 257.0937; found: 257.0938.

*2-(4-(Trifluoromethyl)phenyl)benzo[b]oxepine (**3ab$_2$**).* Yellow solid (46.1 mg, 64%), mp: 126−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.1 Hz, 2 H), 7.66 (d, J = 8.1 Hz, 2 H), 7.33 (t, J = 7.5 Hz, 1 H), 7.21−7.13 (m, 2 H), 7.08 (d, J = 8.1 Hz, 1 H), 6.85 (d, J = 10.8 Hz, 1 H), 6.36−7.28 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 153.2, 138.1, 132.6, 131.8, 130.6, 130.2 (q, J = 32.0 Hz), 129.0, 127.0, 125.5, 125.4 (q, J = 3.0 Hz), 125.0, 122.7, 121.1, 112.1. IR (KBr): 3056, 2987, 1613, 1487, 1329, 1265, 1111, 827, 764 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{12}F_3O$ $[M + H]^+$: 289.0835, found: 289.0831.

*4-(Benzo[b]oxepin-2-yl)-N,N-dimethylaniline (**3ac**).* Yellow solid (59.2 mg, 91%), mp: 120−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.5 Hz, 2 H), 7.31 (t, J = 7.8 Hz, 1 H), 7.21 (d, J = 7.3 Hz, 1 H), 7.13 (dd, J = 12.4, 7.6 Hz, 2 H), 6.80−6.72 (m, 3 H), 6.33 (dd, J = 10.9, 6.3 Hz, 1 H), 6.14 (d, J = 6.2 Hz, 1 H), 3.04 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 154.8, 150.5, 132.4, 129.8, 129.4, 128.4, 128.0, 126.7, 124.5, 122.9, 121.3, 111.8, 106.3, 40.2. IR (KBr): 3023, 2925, 2805, 1610, 1521, 1445, 1362, 1199, 1165, 1048, 944, 816, 758 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{17}NaNO$ $[M + Na]^+$: 286.1202; found: 286.1208.

*4-(4-(Benzo[b]oxepin-2-yl)phenyl)morpholine (**3ad**).* Black solid (64.0 mg, 84%), mp: 83−84 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.6 Hz, 2 H), 7.23 (d, J = 8.5 Hz, 1 H), 7.13 (d, J = 7.2 Hz, 1 H), 7.08 (d, J = 7.2 Hz, 1 H), 7.03 (d, J = 8.0 Hz, 1 H), 6.91 (d, J = 7.4 Hz, 2 H), 6.70 (d, J = 11.0 Hz, 1 H), 6.25 (dd, J = 10.9, 6.2 Hz, 1 H), 6.11 (d, J = 6.2 Hz, 1 H), 3.84 (s, 4 H), 3.18 (s, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 132.2, 130.4, 130.3, 130.0, 129.0, 128.6, 127.7, 126.6, 124.6, 121.2, 115.1, 107.9, 99.8, 66.5, 48.8. IR (KBr): 3024, 2964, 2955, 1596, 1450, 1231, 1189, 1117, 823, 758 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{20}H_{20}NO_2$ $[M + H]^+$: 306.1489; found: 306.1487.

*2-(3,4-Dimethylphenyl)benzo[b]oxepine (**3ae**).* Yellow oil (53.3 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 10.0 Hz, 2 H), 7.25 (t, J = 7.6 Hz, 1 H), 7.13 (d, J = 5.2 Hz, 2 H), 7.07 (dd, J = 12.4, 8.0 Hz, 2 H), 6.73 (d, J = 10.8 Hz, 1 H), 6.26 (dd, J = 10.8, 6.4 Hz, 1 H), 6.19 (d, J = 6.0 Hz, 1 H), 2.27 (d, J = 9.2 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1(4), 155.0(6), 137.5, 136.7, 132.6, 132.3, 131.0, 130.2, 129.9, 128.7, 127.7, 126.7, 124.7, 123.1, 121.4, 109.2, 20.0, 19.7. IR (KBr): 3024, 2969, 2917, 2855, 1634, 1589, 1482, 1448, 1266, 1204, 1020, 820, 754 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{16}NaO$ $[M + Na]^+$: 271.1093; found: 271.1100.

*2-(Naphthalen-2-yl)benzo[b]oxepine (**3af**).* Yellow oil (59.4 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39−8.32 (m, 1 H), 7.83 (t, J = 7.2 Hz, 2 H), 7.63 (d, J = 6.8 Hz, 1 H), 7.50−7.44 (m, 2 H), 7.39 (t, J = 7.6 Hz, 1 H), 7.16 (t, J = 6.8 Hz, 2 H), 7.08 (t, J = 7.2 Hz, 1 H), 6.79 (d, J = 11.2 Hz, 1 H), 6.72 (d, J = 7.6 Hz, 1 H), 6.26 (dd, J = 11.2, 6.0 Hz, 1 H), 5.95 (d, J = 5.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 155.7, 134.3, 133.9, 132.0, 131.6, 131.4, 130.3, 129.5, 128.9, 128.4, 127.4, 127.3, 126.7, 126.4, 126.1, 125.1, 124.9, 121.9, 115.6. IR (KBr): 3054, 2924, 1639, 1483, 1447, 1265, 1202, 1101, 951, 749 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{20}H_{14}NaO$ $[M + Na]^+$: 293.0937; found: 293.0937.

*2-(Furan-2-yl)benzo[b]oxepine (**3ag$_1$**).* Black oil (35.7 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1 H), 7.31 (t, J = 7.6 Hz, 1 H), 7.17−7.11 (m, 2 H), 7.03 (d, J = 8.0 Hz, 1 H), 6.81 (d, J = 2.8 Hz, 1 H), 6.73 (d, J = 11.2 Hz, 1 H), 6.47 (s, 1 H), 6.27 (dd, J = 10.8, 6.4 Hz, 1 H), 6.15 (d, J = 6.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 150.1, 146.6, 143.0, 131.9, 131.2, 130.3, 129.0, 127.1, 125.0, 121.1, 111.6, 108.6, 108.5. HRMS-ESI (m/z): calcd for $C_{14}H_{10}NaO_2$ $[M + Na]^+$: 233.0573; found: 233.0565.

*2-(Thiophen-2-yl)benzo[b]oxepine (**3ag$_2$**).* Yellow oil (33.9 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 3.6 Hz, 1 H), 7.30 (t, J = 7.6 Hz, 1 H), 7.24 (d, J = 4.8 Hz, 1 H), 7.16−7.10 (m, 3 H), 7.03 (t, J = 3.6 Hz, 1 H), 6.73 (d, J = 11.2 Hz, 1 H), 6.22 (dd, J = 11.2, 6.0 Hz, 1 H), 6.10 (d, J = 6.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 150.0, 139.9, 131.8, 131.2, 130.4, 128.9, 127.8, 127.0, 125.8, 125.0, 124.7, 121.3, 108.8. IR (KBr): 3071, 3025, 2922, 2850, 1628, 1516, 1483, 1254, 1196, 822, 750, 697 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{14}H_{10}NaOS$ $[M + Na]^+$: 249.0345; found: 249.0341.

*3-Methyl-2-phenylbenzo[b]oxepine (**3ah$_1$**).* Yellow oil (42.7 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.6 Hz, 2 H), 7.38 (t, J = 7.2 Hz, 2 H), 7.34−7.29 (m, 1 H), 7.21 (t, J = 6.8 Hz, 2 H), 7.10 (t, J = 7.2 Hz, 1 H), 6.85 (d, J = 8.4 Hz, 1 H), 6.80 (d, J = 11.2 Hz, 1 H), 6.27 (d, J = 10.8 Hz, 1 H), 1.93 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 149.1, 136.0, 133.2, 131.5, 130.0, 129.9, 129.1, 128.1(5), 128.1(3), 127.8, 124.4, 121.0, 120.9, 18.8. IR (KBr): 3057, 3018, 2919, 2852, 1641, 1483, 1447, 1264, 1170, 957, 758 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{14}NaO$ $[M + Na]^+$: 257.0937; found: 257.0935.

*2-(4-Methoxyphenyl)-3-methylbenzo[b]oxepine (**3ah$_2$**).* Yellow oil (50.2 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.4 Hz, 2 H), 7.20 (t, J = 7.6 Hz, 2 H), 7.08 (t, J = 7.2 Hz, 1 H), 6.90 (d, J = 8.4 Hz, 2 H), 6.84 (d, J = 8.0 Hz, 1 H), 6.77 (d, J = 11.2 Hz, 1 H), 6.25 (d, J = 11.2 Hz, 1 H), 3.82 (s, 3 H), 1.93 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 155.2, 148.7, 133.4, 131.6, 130.5, 129.9, 129.3, 128.6, 128.1, 124.3, 121.0, 119.7, 113.2, 55.2, 18.9. IR (KBr): 3055, 2987, 2916, 2836, 1605, 1509, 1263, 1170, 837,

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737 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{16}NaO_2$ $[M + Na]^+$: 287.1043; found: 287.1036.

*2,3-Diphenylbenzo[b]oxepine (**3ai$_1$**).*[6] Yellow oil (59.2 mg, 80%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 3.2 Hz, 2 H), 7.32 (d, J = 7.2 Hz, 1 H), 7.24−7.15 (m, 10 H), 6.98 (d, J = 10.8 Hz, 1 H), 6.91 (d, J = 7.6 Hz, 1 H), 6.43 (d, J = 10.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 148.2, 139.2, 135.4, 132.2, 131.4, 130.7, 130.3, 130.1, 129.8, 128.3, 128.1, 127.5, 127.3(2), 127.2(6), 124.6, 121.0. IR (KBr): 3064, 3026, 2925, 2851, 1668, 1595, 1511, 1451, 1383, 1208, 1174, 947, 760 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{22}H_{16}NaO$ $[M + Na]^+$: 319.1093; found: 319.1087.

*2-(4-Fluorophenyl)-3-phenylbenzo[b]oxepine (**3ai$_2$**).* Yellow solid (61.2 mg, 78%), mp: 79−80 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, J = 6.8 Hz, 2 H), 7.30 (d, J = 7.2 Hz, 1 H), 7.24−7.20 (m, 4 H), 7.16−7.12 (m, 3 H), 6.95 (d, J = 11.2 Hz, 1 H), 6.86−6.80 (m, 3 H), 6.38 (d, J = 11.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (d, J = 248.0 Hz), 154.6, 147.2, 139.0, 132.1, 131.8 (d, J = 8.0 Hz), 131.7 (d, J = 3.0 Hz), 131.4, 130.7, 130.4, 130.1, 128.4(4), 128.3(9), 127.4, 127.2, 124.7, 121.0, 114.6 (d, J = 22.0 Hz). IR (KBr): 3057, 3023, 2922, 2851, 1598, 1503, 1446, 1269, 1231, 1174, 841, 758, 700 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{22}H_{15}FNaO$ $[M + Na]^+$: 337.0999; found: 337.0993.

*2-(4-Chlorophenyl)-3-phenylbenzo[b]oxepine (**3ai$_3$**).* Yellow solid (66.8 mg, 81%), mp: 119−120 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.29 (m, 3 H), 7.24−7.21 (m, 4 H), 7.15−7.09 (m, 5 H), 6.95 (d, J = 11.2 Hz, 1 H), 6.85 (d, J = 8.4 Hz, 1 H), 6.37 (d, J = 11.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 146.8, 138.8, 133.9(2), 133.8(9), 132.1, 131.3, 131.1, 131.0, 130.5, 130.0, 128.5, 128.4, 127.9, 127.8, 127.5, 124.8, 120.9. IR (KBr): 3058, 3023, 2958, 2922, 1594, 1484, 1446, 1384, 1208, 1173, 1118, 835, 760, 700 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{22}H_{15}ClNaO$ $[M + Na]^+$: 353.0704; found: 353.0701.

*2-(4-Methoxyphenyl)-3-phenylbenzo[b]oxepine (**3ai$_4$**).* Yellow oil (58.7 mg, 72%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.4 Hz, 2 H), 7.31 (d, J = 7.6 Hz, 1 H), 7.24−7.12 (m, 7 H), 6.94 (d, J = 11.2 Hz, 1 H), 6.89 (d, J = 8.0 Hz, 1 H), 6.69 (d, J = 8.4 Hz, 2 H), 6.40 (d, J = 11.2 Hz, 1 H), 3.75 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 154.5, 148.0, 139.6, 132.4, 131.5, 131.4, 130.2(4), 130.1(5), 130.0, 128.3, 128.2, 128.0, 127.1, 125.9, 124.5, 121.1, 112.9, 55.1. IR (KBr): 3056, 3022, 2959, 2925, 2823, 1603, 1507, 1251, 1172, 1109, 1032, 836, 759, 701 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{23}H_{18}NaO_2$ $[M + Na]^+$: 349.1199; found: 349.1198.

*3-(4-Fluorophenyl)-2-methylbenzo[b]oxepine (**3aj$_1$**).* Yellow oil (47.9 mg, 76%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, J = 7.2 Hz, 1 H), 7.23 (d, J = 7.2 Hz, 1 H), 7.17−7.15 (m, 3 H), 7.02 (t, J = 8.0 Hz, 3 H), 6.77 (d, J = 11.2 Hz, 1 H), 6.20 (d, J = 11.2 Hz, 1 H), 2.05 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9 (d, J = 245.0 Hz), 155.0, 151.8, 135.0 (d, J = 3.0 Hz), 131.4, 131.3, 130.9 (d, J = 8.0 Hz), 130.0, 129.5, 128.5, 124.8, 124.7, 121.1, 115.1 (d, J = 21.0 Hz), 18.8. IR (KBr): 3070, 2959, 2924, 2852, 1598, 1510, 1482, 1221, 1172, 958, 837, 759 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{13}FNaO$ $[M + Na]^+$: 275.0843; found: 275.0843.

*3-(4-Chlorophenyl)-2-methylbenzo[b]oxepine (**3aj$_2$**).* Yellow oil (56.9 mg, 85%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.28 (m, 3 H), 7.23 (d, J = 7.6 Hz, 1 H), 7.18 (d, J = 7.6 Hz, 1 H), 7.13 (d, J = 7.6 Hz, 2 H), 7.02 (d, J = 8.0 Hz, 1 H), 6.78 (d, J = 10.8 Hz, 1 H), 6.18 (d, J = 11.2 Hz, 1 H), 2.05 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 152.0, 137.6, 133.0, 131.3, 131.1, 130.6, 130.0, 129.7, 128.5, 128.4, 124.8, 124.6, 121.1, 18.9. IR (KBr): 3026, 2959, 2924, 2852, 1594, 1486, 1374, 1173, 1090, 760 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{13}ClNaO$ $[M + Na]^+$: 291.0547; found: 291.0553.

*3-(4-Bromophenyl)-2-methylbenzo[b]oxepine (**3aj$_3$**).* Yellow oil (50.7 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2 H), 7.34 (t, J = 7.6 Hz, 1 H), 7.23 (d, J = 7.6 Hz, 1 H), 7.17 (d, J = 7.2 Hz, 1 H), 7.07 (d, J = 8.0 Hz, 2 H), 7.02 (d, J = 8.0 Hz, 1 H), 6.77 (d, J = 11.2 Hz, 1 H), 6.17 (d, J = 11.2 Hz, 1 H), 2.05 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 152.0, 138.1, 131.4, 131.3, 131.0(1), 130.9(9), 129.8, 128.6, 124.8, 124.7, 121.1, 18.93. IR (KBr): 3059, 3023, 2923, 2851, 1642, 1592, 1484, 1384, 1172, 956, 759 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{13}BrNaO$ $[M + Na]^+$: 335.0042; found: 335.0033.

*2-Methyl-3-(p-tolyl)benzo[b]oxepine (**3aj$_4$**).* Yellow oil (47.1 mg, 76%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 7.2 Hz, 1 H), 7.22 (d, J = 8.4 Hz, 1 H), 7.16−7.12 (m, 3 H), 7.08 (d, J = 8.0 Hz, 2 H), 7.01 (d, J = 8.0 Hz, 1 H), 6.75 (d, J = 11.2 Hz, 1 H), 6.22 (d, J = 11.2 Hz, 1 H), 2.33 (s, 3 H), 2.06 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 151.4, 136.7, 136.2, 131.9, 131.5, 129.8, 129.2, 129.1, 128.9, 128.5, 125.4, 124.6, 121.1, 21.1, 18.9. IR (KBr): 3055, 3022, 2917, 2853, 1641, 1595, 1514, 1483, 1264, 1170, 957, 758 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{16}NaO$ $[M + Na]^+$: 271.1093; found: 271.1087.

*3-(4-Methoxyphenyl)-2-methylbenzo[b]oxepine (**3aj$_5$**).* Yellow oil (54.8 mg, 83%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 7.6 Hz, 1 H), 7.22 (d, J = 8.0 Hz, 1 H), 7.15 (d, J = 7.2 Hz, 1 H), 7.11 (d, J = 7.6 Hz, 2 H), 7.02 (d, J = 8.0 Hz, 1 H), 6.85 (d, J = 8.0 Hz, 2 H), 6.75 (d, J = 11.2 Hz, 1 H), 6.21 (d, J = 10.8 Hz, 1 H), 3.79 (s, 3 H), 2.06 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 155.0, 151.2, 131.9, 131.5, 131.4, 130.4, 129.8, 129.1, 128.5, 125.1, 124.6, 121.1, 113.6, 55.2, 18.8. IR (KBr): 3057, 2929, 2836, 1604, 1511, 1244, 1169, 736 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{16}NaO_2$ $[M + Na]^+$: 287.1043, found: 287.1038.

*3-(3-Methoxyphenyl)-2-methylbenzo[b]oxepine (**3ak**).* Yellow oil (47.5 mg, 72%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, J = 7.2 Hz, 1 H), 7.25−7.21 (m, 2 H), 7.16 (t, J = 7.2 Hz, 1 H), 7.02 (d, J = 7.8 Hz, 1 H), 6.81−6.73 (m, 4 H), 6.23 (d, J = 11.2 Hz, 1 H), 3.78 (s, 3 H), 2.06 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 155.1, 151.9, 140.6, 131.5, 131.4, 129.9, 129.3, 129.2, 128.5, 125.5, 124.7, 121.7, 121.1, 114.8, 112.7, 55.3, 19.0. IR (KBr): 3063, 2941, 2908, 2836, 1600, 1485, 1451, 1290, 1214, 1172, 967, 758, 736 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{17}O_2$ $[M + H]^+$: 265.1223, found: 265.1225.

*3-(2-Methoxyphenyl)-2-methylbenzo[b]oxepine (**3al**).* Yellow solid (35.6 mg, 54%), mp: 87−89 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 7.0 Hz, 1H), 7.19 (d, J = 7.3 Hz, 1H), 7.13 (t, J = 7.2 Hz, 1H), 7.02 (dd, J = 13.9, 7.8 Hz, 2H), 6.90 (t, J = 6.5 Hz, 2H), 6.67 (d, J = 11.1 Hz, 1H), 6.17 (d, J = 11.1 Hz, 1H), 3.77 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 155.3, 152.9, 131.9, 131.7, 131.2, 129.5, 128.7, 128.4, 128.3, 127.7, 124.5, 121.6, 121.1, 120.4, 111.2, 55.5, 18.9. IR (KBr): 3068, 3023, 2909, 2834, 1598, 1488, 1456, 1260, 1172, 956, 756 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{16}NaO_2$ $[M + Na]^+$: 287.1043; found: 287.1037.

*2-Isopropyl-3-phenylbenzo[b]oxepine (**3am**).* Yellow solid (52.4 mg, 80%), mp: 115−117 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, J = 7.2 Hz, 2 H), 7.29−7.26 (m, 2 H), 7.20 (d, J = 7.2 Hz, 2 H), 7.13−7.09 (m, 3 H), 6.59 (d, J = 11.2 Hz, 1 H), 6.12 (d, J = 11.2 Hz, 1 H), 2.71−2.64 (m, 1 H), 1.20 (d, J = 6.8 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 157.8, 139.7, 132.3, 131.9, 129.5, 128.9, 128.8, 128.6, 128.4, 126.9, 124.5, 123.9, 121.7, 31.8, 20.7. IR (KBr): 3024, 2966, 2928, 2868, 2637, 1599, 1488, 1446, 1264, 1209, 1046, 958, 761, 700 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{19}H_{18}NaO$ $[M + Na]^+$: 285.1250; found: 285.1244.

*2-Butyl-3-phenylbenzo[b]oxepine (**3an**).* Yellow oil (55.2 mg, 80%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.23 (m, 4 H), 7.16−7.10 (m, 4 H), 7.02 (d, J = 8.0 Hz, 1 H), 6.68 (d, J = 11.2 Hz, 1 H), 6.18 (d, J = 10.8 Hz, 1 H), 2.27 (t, J = 7.6 Hz, 2 H), 1.74−1.67 (m, 2 H), 1.35−1.25 (m, 2 H), 0.85 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 156.0, 139.3, 132.0, 131.6, 129.7, 129.0(4), 129.0(1), 128.5, 128.2, 126.9, 125.6, 124.6, 121.2, 32.3, 29.6, 22.5, 13.8. IR (KBr): 3059, 3024, 2959, 2925, 2858, 1598, 1487, 1205, 1168, 958, 760, 701 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{20}H_{20}NaO$ $[M + Na]^+$: 299.1406; found: 299.1412.

*2-Benzyl-3-phenylbenzo[b]oxepine (**3ao**).* Yellow solid (53.5 mg, 69%), mp: 103−104 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.27 (m, 10 H), 7.21−7.10 (m, 3 H), 6.77 (d, J = 11.2 Hz, 1 H), 6.51 (d, J = 7.6 Hz, 1 H), 6.28 (d, J = 11.2 Hz, 1 H), 3.70 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 154.0, 139.1, 138.3, 131.6, 131.4, 129.8, 129.7, 129.2, 129.1, 128.5, 128.4, 127.3, 126.8, 126.4, 124.6, 121.4, 38.7. IR (KBr): 3056, 3025, 2923, 2851, 1596, 1488, 1264, 960, 738,

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701 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{23}H_{19}O$ $[M + H]^+$: 311.1430; found: 311.1430.

3-(Furan-2-yl)-2-methylbenzo[b]oxepine (**3ap**). Black oil (38.6 mg, 69%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1 H), 7.32 (t, J = 7.6 Hz, 1 H), 7.22 (d, J = 7.2 Hz, 1 H), 7.15 (t, J = 7.2 Hz, 1 H), 7.03 (d, J = 8.0 Hz, 1 H), 6.84 (d, J = 11.2 Hz, 1 H), 6.46−6.34 (m, 2 H), 6.24 (s, 1 H), 2.34 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 153.6, 151.5, 141.6, 131.2, 130.2, 129.9, 128.7, 128.5, 124.9, 121.0, 116.4, 110.9, 108.6, 19.64. IR (KBr): 2998, 2923, 2852, 1670, 1598, 1485, 1449, 1383, 1212, 1177, 1032, 966, 731 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{15}H_{13}O_2$ $[M + H]^+$: 225.0910; found: 225.0910.

2-(2-Methylbenzo[b]oxepin-3-yl)pyridine (**3aq**). Black oil (43.5 mg, 74%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1 H), 7.70 (t, J = 7.2 Hz, 1 H), 7.33−7.26 (m, 2 H), 7.22−7.20 (m, 2 H), 7.15 (t, J = 8.4 Hz, 1 H), 7.01 (d, J = 8.0 Hz, 1 H), 6.84 (d, J = 11.2 Hz, 1 H), 6.40 (d, J = 11.2 Hz, 1 H), 2.17 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 155.1, 155.0, 148.9, 136.8, 131.3, 130.1(4), 130.0(9), 129.9, 128.6, 124.9(4), 124.8(5), 124.6, 121.9, 121.1, 19.27. IR (KBr): 2998, 2922, 2851, 1588, 1484, 1212, 1173, 964, 765 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{16}H_{14}NO$ $[M + H]^+$: 236.1070; found: 236.1070.

3-Benzyl-2-methylbenzo[b]oxepine (**3ar**). Yellow oil (40.9 mg, 66%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.22 (m, 3 H), 7.20−7.08 (m, 5 H), 6.99 (d, J = 8.0 Hz, 1 H), 6.64 (d, J = 11.2 Hz, 1 H), 6.03 (d, J = 11.2 Hz, 1 H), 3.43 (s, 2 H), 2.14 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 151.8, 139.4, 131.8, 131.6, 129.6, 129.4, 128.4, 128.3(2), 128.2(7), 126.1, 124.5, 121.1, 120.9, 37.1, 17.8. IR (KBr): 3055, 2986, 2924, 1639, 1485, 1265, 892, 742 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{16}NaO$ $[M + Na]^+$: 271.1093; found: 271.1095.

2-Ethyl-3-methylbenzo[b]oxepine (**3as**). Yellow oil (31.6 mg, 68%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.23−7.22 (m, 1 H), 7.10−7.05 (m, 2 H), 6.98 (d, J = 8.0 Hz, 1 H), 6.61 (d, J = 11.1 Hz, 1 H), 6.05 (d, J = 11.1 Hz, 1 H), 2.37 (q, J = 7.4 Hz, 2 H), 1.72 (s, 3 H), 1.22 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 155.6, 133.0, 131.7, 129.5, 128.7, 128.2, 124.3, 121.1, 116.9, 25.4, 16.8, 11.9. IR (KBr): 3066, 2925, 2854, 1715, 1589, 1484, 1449, 1268, 1206, 1102, 756 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{13}H_{14}NaO$ $[M + Na]^+$: 209.0937; found: 209.0934.

2-Cyclopropylbenzo[b]oxepine (**3at**). Yellow oil (24.8 mg, 54%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, J = 7.3 Hz, 1 H), 7.09−7.02 (m, 2 H), 6.83 (d, J = 8.1 Hz, 1 H), 6.52 (d, J = 11.1 Hz, 1 H), 6.00 (dd, J = 11.0, 6.1 Hz, 1 H), 5.45 (d, J = 6.0 Hz, 1 H), 1.65−1.57 (m, 1 H), 0.98 (d, J = 2.9 Hz, 2 H), 0.73 (d, J = 6.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 156.1, 132.0, 129.6, 129.5, 128.8, 127.5, 124.6, 121.1, 108.4, 15.0, 5.0. IR (KBr): 3021, 2925, 2852, 1648, 1486, 1383, 1204, 1168, 1046, 943, 754 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{13}H_{13}O$ $[M + H]^+$: 185.0961; found: 185.0971.

1,2,3,4-Tetrahydrodibenzo[b,f]oxepine (**3au**). Yellow oil (38.6 mg, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.21−7.16 (m, 1 H), 7.07−6.99 (m, 2 H), 6.85 (d, J = 8.0 Hz, 1 H), 6.54 (d, J = 11.1 Hz, 1 H), 5.92 (d, J = 11.1 Hz, 1 H), 2.28 (s, 2 H), 2.03 (s, 2 H), 1.63−1.59 (m, 2 H), 1.54−1.50 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 153.1, 131.8, 129.6, 128.9, 128.5, 124.3, 121.1, 119.6, 28.4, 28.2, 22.8, 22.3. IR (KBr): 3022, 2959, 2922, 2849, 1657, 1486, 1449, 1210, 1106, 773 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{14}H_{14}NaO$ $[M + Na]^+$: 221.0937; found: 221.0935.

7,8,9,10-Tetrahydro-6H-benzo[b]cyclohepta[f]oxepine (**3av**). Yellow oil (37.6 mg, 71%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.27−7.25 (m, 1 H), 7.14−7.07 (m, 2 H), 6.96 (d, J = 8.0 Hz, 1 H), 6.60 (d, J = 10.9 Hz, 1 H), 6.08 (d, J = 11.0 Hz, 1 H), 2.59 (d, J = 8.0 Hz, 2 H), 2.17 (d, J = 8.6 Hz, 2 H), 1.70−1.57 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 155.5, 133.5, 131.5, 129.5, 128.2(1), 128.1(5), 125.1, 124.3, 120.7, 34.6, 31.1, 31.0, 26.4, 25.3. IR (KBr): 2927, 1668, 1568, 1461, 1392, 1227, 1159, 1023, 758 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{15}H_{16}NaO$ $[M + Na]^+$: 235.1093, found: 235.1095.

(Z)-6,7,8,9,10,11-Hexahydrobenzo[b]cyclooct[f]oxepine (**3aw**). Yellow oil (40.7 mg, 72%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, J = 7.4 Hz, 1 H), 7.11−7.05 (m, 2 H), 6.98 (d, J = 8.0 Hz, 1 H), 6.64 (d, J = 11.1 Hz, 1 H), 6.05 (d, J = 11.1 Hz, 1 H), 2.48 (d, J = 6.0 Hz, 2 H), 2.17 (d, J = 6.0 Hz, 2 H), 1.70−1.67 (m, 2 H), 1.57−1.51 (m, 2 H), 1.41 (t, J = 9.0 Hz, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 154.2, 131.9, 131.4, 129.5, 129.3, 128.2, 124.2, 122.1, 120.9, 32.2, 30.4, 29.6, 29.1, 26.4, 26.0. IR (KBr): 3016, 2923, 2851, 1598, 1485, 1449, 1206, 1110, 969, 762 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{16}H_{18}NaO$ $[M + Na]^+$: 249.1250; found: 249.1251.

12,13-Dihydrobenzo[b]naphtho[1,2-f]oxepine (**3ax**). Yellow solid (50.4 mg, 82%), mp: 97−98 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 1 H), 7.78 (d, J = 8.0 Hz, 1 H), 7.67 (d, J = 8.8 Hz, 1 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.39 (t, J = 7.6 Hz, 2 H), 7.14−7.24 (m, 3 H), 7.06 (t, J = 7.2 Hz, 1 H), 3.50−3.47 (m, 2 H), 3.32−3.29 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 154.4, 133.5, 133.3, 130.7, 129.5, 128.5, 127.9, 127.3, 126.4, 124.4(2), 124.3(7), 123.5, 123.0, 122.0, 120.6, 29.8, 27.4. IR (KBr): 2959, 2925, 2825, 1636, 1460, 1380, 1266, 1080, 760 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{15}O$ $[M + H]^+$: 247.1117, found: 247.1117.

8-Chloro-2-phenylbenzo[b]oxepine (**3ba**). Yellow solid (57.1 mg, 90%), mp: 75−76 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.3 Hz, 2 H), 7.43 (t, J = 7.3 Hz, 2 H), 7.39−7.33 (m, 1 H), 7.15−7.06 (m, 3 H), 6.73 (d, J = 10.1 Hz, 1 H), 6.32−6.27 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 154.6, 135.3, 134.3, 130.7, 130.4, 129.3, 128.8, 128.6, 127.7, 125.3, 125.1, 121.7, 110.2. IR (KBr): 3027, 2923, 2851, 1588, 1482, 1270, 1078, 1043, 824, 765, 721 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{16}H_{11}ClNaO$ $[M + Na]^+$: 277.0391; found: 277.0393.

8-Chloro-3-(4-chlorophenyl)-2-methylbenzo[b]oxepine (**3bj$_2$**). Yellow solid (66.4 mg, 88%), mp: 91−93 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.2 Hz, 2H), 7.18−7.10 (m, 4 H), 7.05 (s, 1 H), 6.72 (d, J = 11.1 Hz, 1 H), 6.18 (d, J = 11.1 Hz, 1 H), 2.05 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 151.9, 137.1, 135.1, 133.1, 131.4, 130.5, 129.8, 129.1, 128.7, 128.5, 125.1, 124.8, 121.6, 18.8. IR (KBr): 3028, 2911, 1591, 1483, 1174, 1085, 964, 834 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{12}Cl_2NaO$ $[M + Na]^+$: 325.0157, found: 325.0159.

8-Bromo-2-phenylbenzo[b]oxepine (**3ca**). Yellow solid (66.3 mg, 89%), mp: 87−88 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.4 Hz, 2 H), 7.41−7.32 (m, 3 H), 7.24−7.22 (m, 2 H), 7.00 (d, J = 7.9 Hz, 1 H), 6.69 (d, J = 10.7 Hz, 1 H), 6.31−6.23 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 154.7, 134.3, 131.1, 130.5, 129.6, 128.9, 128.6, 128.0, 127.9, 125.4, 124.6, 123.1, 110.2. IR (KBr): 3026, 2922, 2853, 1583, 1480, 1269, 1040, 920, 821, 764 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{16}H_{11}BrNaO$ $[M + Na]^+$: 320.9885; found: 320.9885.

8-Bromo-3-(4-chlorophenyl)-2-methylbenzo[b]oxepine (**3cj$_2$**). Yellow solid (72.8 mg, 82%), mp: 97.2−98.7 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.3 Hz, 3 H), 7.20 (s, 1 H), 7.13−7.07 (m, 3 H), 6.70 (d, J = 11.1 Hz, 1 H), 6.19 (d, J = 11.1 Hz, 1 H), 2.04 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 152.0, 137.1, 133.1, 131.5, 130.5, 130.3, 129.4, 128.7, 128.5, 128.0, 124.8, 124.5, 122.9, 18.8. IR (KBr): 3033, 2930, 2858, 1582, 1478, 1167, 1088, 957, 801 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{12}BrNaClO$ $[M + Na]^+$: 368.9652, found: 368.9653.

2-Phenylbenzo[b]oxepine-8-carbonitrile (**3da**). Yellow solid (52.7 mg, 86%), mp: 113−114 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.1 Hz, 2 H), 7.48−7.40 (m, 4 H), 7.37 (s, 1 H), 7.28 (d, J = 3.5 Hz, 1 H), 6.79 (d, J = 11.0 Hz, 1 H), 6.46 (dd, J = 11.0, 6.3 Hz, 1 H), 6.34 (d, J = 6.3 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 154.5, 137.0, 133.9, 130.6, 129.9, 129.4, 128.7, 128.5, 125.5, 125.2, 118.1, 113.1, 110.0. IR (KBr): 3027, 2920, 1600, 1489, 1226, 887, 834 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{11}NNaO$ $[M + Na]^+$: 268.0733, found: 268.0735.

3-(4-Chlorophenyl)-2-methylbenzo[b]oxepine-8-carbonitrile (**3dj$_2$**). Yellow solid (60.8 mg, 83%), mp: 160−162 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.8 Hz, 1 H), 7.32−7.26 (m, 4 H), 7.11 (d, J = 8.2 Hz, 2 H), 6.73 (d, J = 11.2 Hz, 1 H), 6.30 (d, J = 11.2 Hz, 1 H), 2.05 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 153.0, 136.6, 136.1, 134.1, 133.4, 130.4, 129.2, 128.6, 128.5, 128.2, 124.8(8), 124.8(6), 118.1, 112.9, 18.9. IR (KBr): 2024, 2920, 1600, 1546, 1490, 1168, 1089, 976, 833 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{18}H_{12}ClNNaO$ $[M + Na]^+$: 316.0500; found: 316.0507.

8-Methyl-2-phenylbenzo[b]oxepine (**3ea**). Yellow solid (46.8 mg, 80%), mp: 73−75 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.1 Hz, 2 H), 7.38 (t, J = 7.7 Hz, 2 H), 7.33−7.29 (m, 1 H), 7.03

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(d, J = 7.6 Hz, 1 H), 6.91 (d, J = 10.4 Hz, 2 H), 6.73 (d, J = 10.1 Hz, 1 H), 6.27−6.18 (m, 2 H), 2.29 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 154.4, 140.9, 134.9, 131.4, 129.2, 128.5, 128.4(7), 128.4(5), 126.5, 125.5, 125.4, 121.7, 110.2, 21.0. IR (KBr): 3026, 2922, 2853, 1607, 1497, 1448, 1266, 1323, 1150, 1045, 822, 769 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{15}O$ $[M + H]^+$: 235.1117; found: 235.1116.

*7-Methyl-2-phenylbenzo[b]oxepine (**3fa**).* Yellow oil (48.0 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.1 Hz, 2 H), 7.40 (t, J = 7.4 Hz, 2 H), 7.36−7.30 (m, 1 H), 7.10 (d, J = 8.2 Hz, 1 H), 6.99 (d, J = 7.1 Hz, 2 H), 6.76 (d, J = 10.1 Hz, 1 H), 6.28 (q, J = 6.1 Hz, 2 H), 2.31 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 153.1, 134.8, 134.2, 131.6, 131.5, 130.9, 129.1, 128.5, 128.4, 127.4, 125.4, 120.9, 110.0, 20.6. IR (KBr): 3024, 2922, 2854, 1599, 1491, 1447, 1202, 752, 691 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{17}H_{14}NaO$ $[M + Na]^+$: 257.0937; found: 257.0934.

*2-Phenyloxepino[2,3-b]pyridine (**3ga**).* Yellow oil (32.1 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, J = 4.8, 1.8 Hz, 1 H), 8.05−7.97 (m, 2 H), 7.55 (dd, J = 7.4, 1.8 Hz, 1 H), 7.43−7.39 (m, 2 H), 7.35−7.32 (m, 1 H), 7.12 (dd, J = 7.4, 4.8 Hz, 1 H), 6.67−6.59 (m, 1 H), 6.38−6.31 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 154.6, 148.7, 137.9, 134.7, 128.9, 128.6, 128.6, 128.3, 126.6, 126.0, 121.3, 109.5. IR (KBr): 3056, 2922, 2852, 1635, 1575, 1491, 1425, 1270, 1146, 732 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{15}H_{12}NO$ $[M + H]^+$: 222.0913; found: 222.0911.

*(E)-4-(2-Fluorophenyl)-1-(furan-2-yl)but-3-en-1-one (**4ag$_1$**).* Yellow oil (23.6 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 5.0 Hz, 1 H), 7.46 (t, J = 7.7 Hz, 1 H), 7.25 (d, J = 3.6 Hz, 1 H), 7.20−7.16 (m, 1H), 7.09−6.98 (m, 2 H), 6.72 (d, J = 16.2 Hz, 1 H), 6.56−6.45 (m, 2H), 3.78 (d, J = 7.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.6, 161.0 (d, J = 248.0 Hz), 152.3, 146.5, 128.8 (d, J = 9.0 Hz), 127.2 (d, J = 4.0 Hz), 126.2 (d, J = 4.0 Hz), 124.6 (d, J = 12.0 Hz), 124.4 (d, J = 4.0 Hz), 124.0 (d, J = 3.0 Hz), 117.6, 115.5 (d, J = 20.0 Hz), 112.3, 42.9. IR (KBr): 30211, 2925, 1585, 1488, 1450, 1226, 1100, 1034, 755 cm^{-1}. HRMS-ESI (m/z): calcd for $C_{14}H_{11}FNaO_2$ $[M + Na]^+$: 253.0635, found: 253.0635.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02487.

^{1}H and ^{13}C NMR spectra of all synthesized compounds (PDF)

X-ray structure and crystallographic data for compound **3ai$_3$** (CIF)

X-ray structure and crystallographic data for compound **3ax** (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Spiteller, P. *Chem. - Eur. J.* **2008**, *14*, 9100. (b) Bakthadoss, M.; Sivakumar, N.; Devaraj, A. *Tetrahedron Lett.* **2015**, *56*, 4980. (c) Ren, Y.; Kardono, L. B. S.; Riswan, S.; Chai, H.; Farnsworth, N. R.; Soejarto, D. D.; Carcache de Blanco, E. J.; Kinghorn, A. D. *J. Nat. Prod.* **2010**, *73*, 949. (d) Yamaguchi, S.; Tsuchida, N.; Miyazawa, M.; Hirai, Y. *J. Org. Chem.* **2005**, *70*, 7505.

(2) (a) Vyvyan, J. R.; Looper, R. E. *Tetrahedron Lett.* **2000**, *41*, 1151. (b) El Marsni, Z.; Torres, A.; Varela, R. M.; Molinillo, J. M. G.; Casas, L.; Mantell, C.; de la Ossa, E. J. M.; Macias, F. A. *J. Agric. Food Chem.* **2015**, *63*, 6410. (c) Macías, F. A.; Varela, R. M.; Torres, A.; Molinillo, M. G. *Tetrahedron Lett.* **1999**, *40*, 4725.

(3) For related reviews on the synthesis of oxepines, see: (a) Hoberg, J. O. *Tetrahedron* **1998**, *54*, 12631. (b) Snyder, N. L.; Haines, H. M.; Peczuh, M. W. *Tetrahedron* **2006**, *62*, 9301.

(4) (a) Varela-Fernández, A.; García-Yebra, C.; Varela, J. A.; Esteruelas, M. A.; Saá, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 4278. (b) Chan, P. W. H.; Teo, W. T.; Koh, S. W. Y.; Lee, B. R.; Ayers, B. J.; Ma, D.-L.; Leung, C.-H. *Eur. J. Org. Chem.* **2015**, *2015*, 4447. (c) Coulter, M. M.; Dornan, P. K.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 6932. (d) Calder, E. D. D.; Sharif, S. A. I.; McGonagle, F. I.; Sutherland, A. *J. Org. Chem.* **2015**, *80*, 4683. (e) Bera, K.; Jalal, S.; Sarkar, S.; Jana, U. *Org. Biomol. Chem.* **2014**, *12*, 57. (f) Sze, E. M. L.; Rao, W.; Koh, M. J.; Chan, P. W. H. *Chem. - Eur. J.* **2011**, *17*, 1437. (g) Liu, J.; Liu, Y. *Org. Lett.* **2012**, *14*, 4742. (h) Ramachary, D. B.; Narayana, V. V.; Ramakumar, K. *Eur. J. Org. Chem.* **2008**, *2008*, 3907.

(5) (a) Lautens, M.; Paquin, J.-F.; Piguel, S. *J. Org. Chem.* **2002**, *67*, 3972. (b) Liu, G.; Lu, X. *Adv. Synth. Catal.* **2007**, *349*, 2247. (c) Yu, X.; Lu, X. *J. Org. Chem.* **2011**, *76*, 6350. (d) Sun, L.-L.; Hu, B.-L.; Tang, R.-Y.; Deng, C.-L.; Zhang, X.-G. *Adv. Synth. Catal.* **2013**, *355*, 377. (e) Friedman, A. A.; Panteleev, J.; Tsoung, J.; Huynh, V.; Lautens, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 9755.

(6) Seoane, A.; Casanova, N.; Quiñones, N.; Mascareñas, J. L.; Gulías, M. *J. Am. Chem. Soc.* **2014**, *136*, 834.

(7) (a) Choi, Y. L.; Lim, H. S.; Lim, H. J.; Heo, J.-N. *Org. Lett.* **2012**, *14*, 5102. (b) Gharpure, S. J.; Reddy, S. R. B. *Eur. J. Org. Chem.* **2013**, *2013*, 2981.

(8) For selective reviews on transition-metal-free coupling reactions, see: (a) Sun, C.-L.; Shi, Z.-J. *Chem. Rev.* **2014**, *114*, 9219. (b) Mehta, V. P.; Punji, B. *RSC Adv.* **2013**, *3*, 11957. (c) Narayan, R.; Matcha, K.; Antonchick, A. P. *Chem. - Eur. J.* **2015**, *21*, 14678.

(9) (a) He, H.; Qi, C.; Hu, X.; Ouyang, L.; Xiong, W.; Jiang, H. *J. Org. Chem.* **2015**, *80*, 4957. (b) He, H.; Qi, C.; Ou, Y.; Xiong, W.; Hu, X.; Ren, Y.; Jiang, H. *Org. Biomol. Chem.* **2014**, *12*, 8128. (c) Qi, C.; Jiang, H.; Huang, L.; Yuan, G.; Ren, Y. *Org. Lett.* **2011**, *13*, 5520. (d) Gao, Y.; Xiong, W.; Chen, H.; Wu, W.; Peng, J.; Gao, Y.; Jiang, H. *J. Org. Chem.* **2015**, *80*, 7456. (e) Li, J.; Yang, W.; Yang, S.; Huang, L.; Wu, W.; Sun, Y.; Jiang, H. *Angew. Chem., Int. Ed.* **2014**, *53*, 7219. (f) Huang, L.; Jiang, H.; Qi, C.; Liu, X. *J. Am. Chem. Soc.* **2010**, *132*, 17652.

(10) CCDC-1422544 and CCDC-1423097 contain the supplementary crystallographic data for compounds **3ai$_3$** and **3ax**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(11) (a) Trofimov, B. A.; Schmidt, E. Y.; Ushakov, I. A.; Zorina, N. V.; Skital'tseva, E. V.; Protsuk, N. I.; Mikhaleva, A. I. *Chem. - Eur. J.* **2010**, *16*, 8516. (b) Trofimov, B. A.; Schmidt, E. Y.; Zorina, N. V.; Ivanova, E. V.; Ushakov, I. A. *J. Org. Chem.* **2012**, *77*, 6880. (c) Trofimov, B. A.; Schmidt, E. Y.; Zorina, N. V.; Ivanova, E. V.; Ushakov, I. A.; Mikhaleva, A. I. *Adv. Synth. Catal.* **2012**, *354*, 1813.

(12) (a) Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119. (b) Sawyer, J. S. *Tetrahedron* **2000**, *56*, 5045.

(13) (a) Thorand, S.; Krause, N. *J. Org. Chem.* **1998**, *63*, 8551. (b) Pearson, A. J.; Kim, J. B. *Tetrahedron Lett.* **2003**, *44*, 8525.

(14) Igeta, H.; Arai, H.; Hasegawa, H.; Tsuchiya, T. *Chem. Pharm. Bull.* **1975**, *23*, 2791.

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