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A Facile One-Pot Access to Dibenzo[*b*,*e*]oxepines by a Lewis Acid Catalysed Tandem Reaction

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Dibenzo[*b*,*e*]oxepine derivatives have been constructed efficiently by one-pot tandem carbon–carbon bond formation reactions. First, 2-(3,5-dimethoxybenzyloxy)benzaldehydes were treated with various nucleophiles under I_2 catalysis and then 1-(3,5-dimethoxybenzyloxy)-3,5-dimethoxybenzene was treated with several aromatic as well as heteroaromatic aldehydes under $BF_3{\cdot}Et_2O$ catalytic conditions to provide dibenzo[*b*,*e*]oxepines in good yields.

Introduction

Dibenzoxepine is an important structural motif in various pharmaceuticals with remarkable diverse biological activities.[1] For instance, Doxepine, a dibenzoxepine tricyclic compound, is most commonly used orally as an anti-depressant[2] and Olopatadine, an anti-histamine, anti-cholinergic and mast cell stabilizer, is used to treat the symptoms of allergic pink eye (Figure 1).[3] Dibenzoxepines have also been used as inhibitors of acyl-CoA, anti-allergic agents and non-prostenoid thrombaxane A_2 receptor antagonists.[4] In addition, these scaffolds are found in bioactive natural products.[5] As a result of their importance, dibenzoxepines are synthetic targets of many researchers. The familiar approaches to synthesizing the dibenzoxepine ring system are the palladium-catalysed cascade carbometallation/cross-coupling of alkynes, preparation of the 11-oxo scaffold followed by Wittig reaction or dehydration of carbinols and others.[6,7] Most of these methods provide dibenzo[*b*,*e*]oxepine compounds containing an exocyclic olefin substitution at the C-11 carbon. Thus, development of efficient methods for the synthesis of dibenzoxepines with various functional groups is highly desirable.

Our recent studies have focused on the use of benzylic/propargylic alcohols as alkylating agents in carbon–carbon, carbon–nitrogen and carbon–oxygen bond-forming reactions for the synthesis of heterocyclic compounds. For example, the C-3 alkylation of 4-hydroxycoumarin to yield furanocoumarins, the synthesis of pyrazoles by the *N*-alkylation of tosylhydrazones and the alkylation of 1,3-dicarbonyl compounds to give various oxygenated heterocycles have been successfully demonstrated.[8] To further extend the use of benzylic alcohols, in particular, by generating them in situ, we became interested in the synthesis of dibenzoxepine derivatives. This was envisioned by a cascade sequence of nucleophilic addition to (benzyloxy)benzaldehyde/intramolecular Friedel–Crafts alkylation or vice versa to give the 6,11-dihydrodibenzoxepine derivative (Scheme 1). To the best of our knowledge there are no such one-pot methods available for the synthesis of dibenzoxepines. While this work was in progress, two papers appeared reporting a similar concept for the synthesis of xanthenes and in one of the reports a single example of dibenzoxepine was achieved in 48% yield using a different substrate.[9] Furthermore, the synthesis of 6,11-dihydrodibenzoxepines is much less studied.[4c,10] The above observations combined with our interest prompted us to explore a one-pot tandem

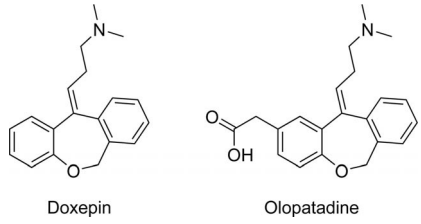
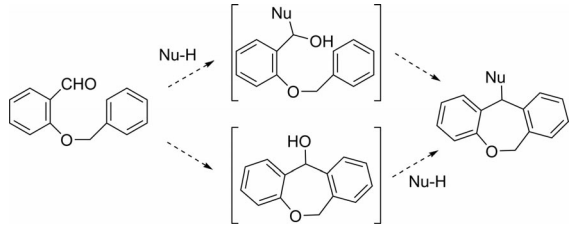


Figure 1. Structures of doxepine and olopatadine.



Scheme 1. Proposed cascade sequence.

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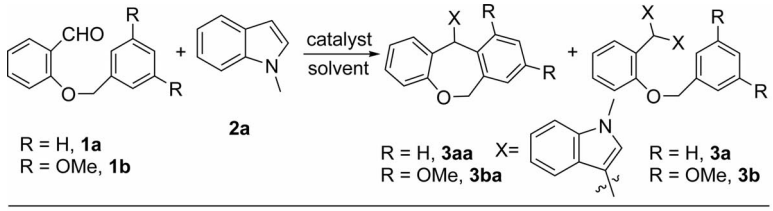
reaction towards 6,11-dihydrodibenzoxepines and the results are described in this paper.

Results and Discussion

Initially we investigated the possibility of a one-pot tandem nucleophilic addition/Friedel–Crafts cyclization on 2-(benzyloxy)benzaldehyde (**1a**), which was easily obtained by the *O*-benzylation of salicylaldehyde using benzyl bromide/K_2CO_3 in DMF. The reaction of **1a** was carried out with *N*-methylindole (**2a**) in the presence of $BF_3{\cdot}Et_2O$ (10 mol-%) in dichloromethane at room temperature. However, the reaction did not give the expected dibenzoxepine **3aa**, instead triarylmethane **3a** was obtained in 46% yield (entry 1, Table 1). The same reaction using other acid catalysts such as $FeCl_3$, $B(C_6F_5)_3$, molecular iodine and *p*TSA in dichloromethane also provided **3a** (entries 2–5, Table 1). As gold catalysts are gaining prominence,[11] we also tested the one-pot tandem reaction using $AuCl_3$ (entry 6, Table 1). These results clearly demonstrate that, after the initial nucleophilic addition of *N*-methylindole to **1a**, no intramolecular cyclization takes place, instead **3a** obtained by S_N1 nucleophilic substitution with **2a**. This may be due to the less nucleophilic nature of the phenyl ring present in the benzyl group. Subsequently, we thought that a more electron-rich substrate may be better suited for the proposed tandem reaction. To ensure this, we prepared 2-(3,5-dimethoxybenzyloxy)benzaldehyde (**1b**) by the *O*-benzylation of salicylaldehyde using 3,5-dimethoxybenzyl bromide/K_2CO_3 in DMF. The reaction of **1b** was first studied with *N*-methylindole (**2a**) in the presence of $BF_3{\cdot}Et_2O$ (10 mol-%) in dichloromethane at room temp. The cyclized product, dibenzoxepine derivative **3ba**, was obtained in 65% yield (entry 7, Table 1). When the reaction temperature was raised to reflux, there was no improvement in yield. Encouraged by the above result, to optimize the reaction conditions, the reaction of **1b** with **2a** was carried out in the presence of various acid catalysts such as $FeCl_3$, $B(C_6F_5)_3$, molecular iodine, *p*TSA and $AuCl_3$. Among the acid catalysts screened, 10 mol-% of molecular iodine provided 67% yield of **3ba** whereas the other catalysts afforded the product in lower yields (entries 8–12, Table 1). However, changing the solvent from CH_2Cl_2 to CH_3CN facilitated an improvement in the yield to 84% in the case of 10 mol-% I_2, but no improvement in yield was observed for $BF_3{\cdot}E_2O$, *p*TSA or $AuCl_3$ (entries 13–16, Table 1).

Having demonstrated the viability of this catalytic strategy in obtaining **3ba**, we next explored the scope of the transformation under the optimized conditions (10 mol-% of I_2, CH_3CN, room temp.). Thus, the reaction of aldehyde **1b** with several nucleophiles was studied and the results are summarized in Table 2. Various electron-rich aromatics

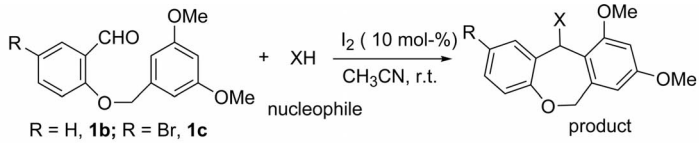
Table 1. Optimization of the conditions for the reactions of **1a** and **1b** with **2a**.[a]

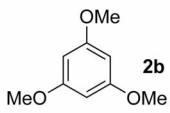
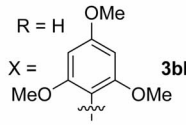
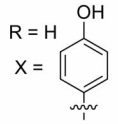
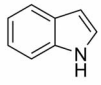
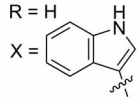
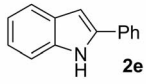
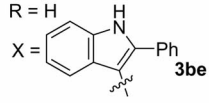
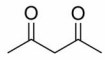
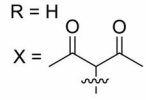
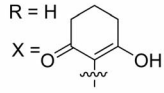
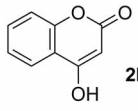
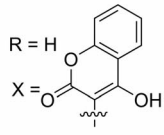
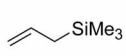
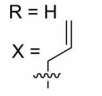
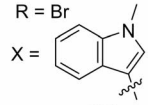
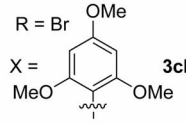
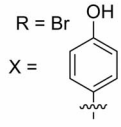
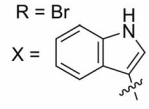


Entry	Reactants	Catalyst	Solvent	Time (h)	Product/Yield (%)[b]	
1	**1a** + **2a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	12	**3aa**/0	**3a**/46
2	**1a** + **2a**	$FeCl_3$	CH_2Cl_2	8	**3aa**/0	**3a**/38
3	**1a** + **2a**	$B(C_6F_5)_3$	CH_2Cl_2	14	**3aa**/0	**3a**/43
4	**1a** + **2a**	I_2	CH_2Cl_2	8	**3aa**/0	**3a**/45
5	**1a** + **2a**	*p*TSA	CH_2Cl_2	10	**3aa**/0	**3a**/41
6	**1a** + **2a**	$AuCl_3$	CH_2Cl_2	6	**3aa**/0	**3a**/42
7	**1b** + **2a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	12	**3ba**/65	**3b**/0
8	**1b** + **2a**	$FeCl_3$	CH_2Cl_2	9	**3ba**/38	**3b**/0
9	**1b** + **2a**	$B(C_6F_5)_3$	CH_2Cl_2	16	**3ba**/32	**3b**/0
10	**1b** + **2a**	I_2	CH_2Cl_2	10	**3ba**/67	**3b**/0
11	**1b** + **2a**	*p*TSA	CH_2Cl_2	9	**3ba**/61	**3b**/0
12	**1b** + **2a**	$AuCl_3$	CH_2Cl_2	8	**3ba**/62	**3b**/0
13	**1b** + **2a**	I_2	CH_3CN	8	**3ba**/84	**3b**/0
14	**1b** + **2a**	$BF_3{\cdot}Et_2O$	CH_3CN	10	**3ba**/63	**3b**/0
15	**1b** + **2a**	*p*TSA	CH_3CN	9	**3ba**/60	**3b**/0
16	**1b** + **2a**	$AuCl_3$	CH_3CN	10	**3ba**/65	**3b**/0

[a] Reactions were carried out under N_2 with 10 mol-% catalyst at room temp. [b] Isolated yields based on **1a** or **1b** used.

Table 2. Synthesis of 11-substituted dibenzo[*b*,*e*]oxepines by iodine-catalysed tandem cyclization.

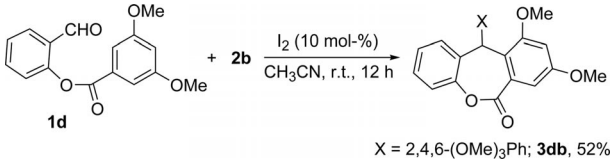


Entry	Substrate	Nucleophile (XH)	Time (h)	Product	Yield (%)[a]
1	**1b**	 **2b**	10	 **3bb**	67
2	**1b**	 **2c**	12	 **3bc**	68
3	**1b**	 **2d**	12	 **3bd**	68
4	**1b**	 **2e**	7	 **3be**	80
5	**1b**	 **2f**	8	 **3bf**	74
6	**1b**	 **2g**	10	 **3bg**	76
7	**1b**	 **2h**	4	 **3bh**	88
8	**1b**	 **2i**	6	 **3bi**	64
9	**1c**	**2a**	6	 **3ca**	76
10	**1c**	**2b**	6	 **3cb**	67
11	**1c**	**2c**	12	 **3cc**	64
12	**1c**	**2d**	5	 **3cd**	73

[a] Isolated yields.

such as 1,3,5-trimethoxybenzene (**2b**), phenol (**2c**), indole (**2d**) and 2-phenylindole (**2e**) served as nucleophiles to provide the corresponding 11-substituted dibenzo[*b*,*e*]oxepines **3bb**–**be** in good yields of between 67 and 80% (entries 1–

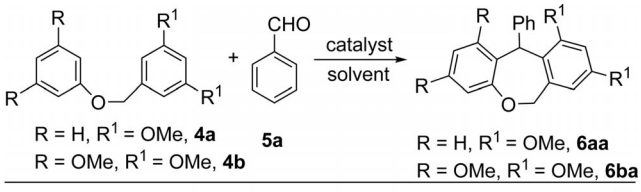
4, Table 2). In addition, 1,3-dicarbonyl compounds such as acetylacetone (**2f**), 1,3-cyclohexanedione (**2g**) and 4-hydroxycoumarin (**2h**) are also found to be well suited for this I_2-catalysed tandem reaction, giving the corresponding products **3bf**, **3bg** and **3bh** in 74, 76 and 88% yields, respectively (entries 5–7, Table 2). Note that allyltrimethylsilane was successfully used as a nucleophile to obtain 11-allyldibenzoxepine (**3bi**) in 64% yield (entry 8, Table 2). To further expand the range of substrates, we decided to use bromo-substituted benzyloxybenzaldehyde **1c**, which will be useful for preparing further analogues by palladium coupling reactions. Accordingly, aldehyde **1c** was treated with *N*-methylindole (**2a**) under I_2 catalysis to yield (76%) the dibenzoxepine **3ca** in 6 h (entry 9, Table 2). The reaction of **1c** with 1,3,5-trimethoxybenzene (**2b**), phenol (**2c**) and indole (**2d**) furnished the corresponding products **3cb**, **3cc** and **3cd** in 67, 64 and 73% yields, respectively (entries 10–12, Table 2). Finally, a different substrate **1d**, derived from salicylaldehyde and 3,5-dimethoxybenzoic acid, was also tested; **1d** underwent the cascade cyclization reaction with 1,3,5-trimethoxybenzene (**2b**) to afford the 11-substituted dibenzo[*b*,*e*]oxepin-6(11*H*)-one **3db** in 52% yield (Scheme 2).



Scheme 2. Reaction of **1d** of 1,3,5-trimethoxybenzene.

In addition, we were interested in knowing whether a benzyl ether and an external aldehyde could be used as substrates to prepare similar 11-substituted dibenzo[*b*,*e*]oxepine derivatives. For this reason, two different benzyl ethers **4a** and **4b** were prepared by the alkylation of phenol and 3,5-dimethoxyphenol with 3,5-dimethoxybenzyl bromide. Once the benzyl ethers **4a** and **4b** were in hand, we focused our attention on studying their reactivity with benzaldehyde to obtain the desired products. As presented in Table 3, when 1,3-dimethoxy-5-(phenoxymethyl)benzene (**4a**) and benzaldehyde (**5a**) in I_2 (10 mol-%) and acetonitrile were allowed to react at room temp. for 12 h, a complex inseparable mixture of products along with the starting material were obtained, showing the reaction is not clean (entry 1, Table 3). However, the strongly electron-rich substrate 1-(3,5-dimethoxybenzyloxy)-3,5-dimethoxybenzene (**4b**) provided 1,3,8,10-tetramethoxy-11-phenyl-6,11-dihydrodibenzo[*b*,*e*]-oxepine (**6ba**) in 71% yield in 6 h (entry 2, Table 3).

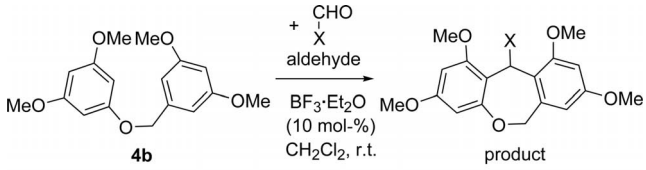
Table 3. Optimization of the conditions for the reactions of **4a** and **4b** with **5a**.[a]

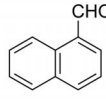
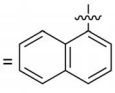
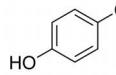
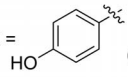
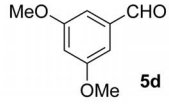
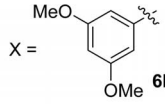
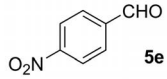
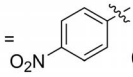
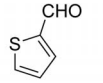
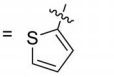
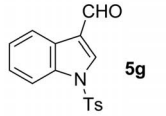
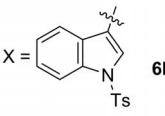
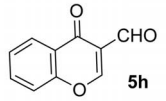
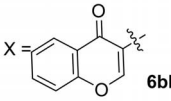
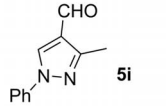
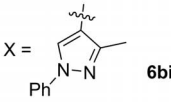
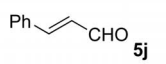
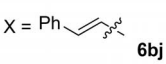
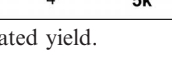
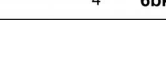


Entry	Reactants	Catalyst	Solvent	Time (h)	Product/Yield (%)[b]
1	**4a** + **5a**	I_2	CH_3CN	16	complex mixture
2	**4b** + **5a**	I_2	CH_3CN	6	**6ba**/71
3	**4b** + **5a**	*p*TSA	CH_3CN	4	**6ba**/68
4	**4b** + **5a**	$BF_3{\cdot}Et_2O$	CH_3CN	3	**6ba**/78
5	**4b** + **5a**	$ZnCl_2$	CH_3CN	8	**6ba**/48
6	**4b** + **5a**	$AuCl_3$	CH_3CN	12	**6ba**/15
7	**4b** + **5a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	1	**6ba**/84

[a] Reactions were carried out under N_2 with 10 mol-% catalyst at room temp. [b] Isolated yields based on **4a** or **4b** used.

Table 4. Synthesis of 11-substituted dibenzo[*b*,*e*]oxepines by $BF_3{\cdot}Et_2O$-catalysed tandem cyclization.



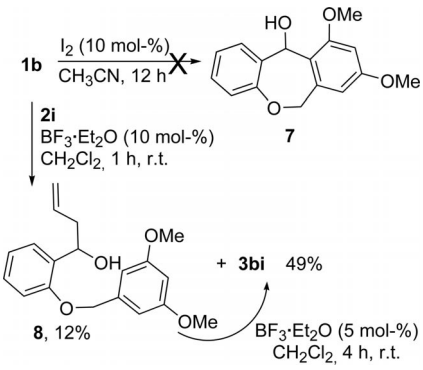
Entry	Aldehyde	Time (h)	Product	Yield (%)[a]
1	 **5b**	4	X =  **6bb**	70
2	 **5c**	3	X =  **6bc**	74
3	 **5d**	3	X =  **6bd**	75
4	 **5e**	1	X =  **6be**	78
5	 **5f**	7	X =  **6bf**	65
6	 **5g**	9	X =  **6bg**	90
7	 **5h**	1	X =  **6bh**	92
8	 **5i**	5	X =  **6bi**	72
9	 **5j**	8	X =  **6bj**	60
10	 **5k**	12	X =  **6bk**	0

[a] Isolated yield.

Furthermore, we examined the reaction of **4b** with **5a** under different conditions to check for improvements in the yield of the desired product. Catalysts such as *p*TSA, $BF_3{\cdot}Et_2O$ and $ZnCl_2$ in CH_3CN provided similar results to those obtained with I_2/CH_3CN (entries 3–5, Table 3), but $AuCl_3$ provided a low yield of the product (entry 6, Table 3). Interestingly, the reaction of **4b** with **5a** was complete in 1 h with $BF_3{\cdot}Et_2O$ in CH_2Cl_2, with **6ba** obtained in 84% yield (entry 6, Table 3).

Under the above optimized conditions, we then focused on the reaction of various aldehydes with **4b**. As indicated in Table 4, benzaldehydes with electron-donating and -withdrawing groups **5b**–**5e** underwent successful cascade reactions to furnish the corresponding 11-aryldibenzo[*b*,*e*]oxepines **6bb**–**6be** in good yields of between 70 and 80% (entries 1–4, Table 4). Similarly, heterocyclic aldehydes such as thiophene-2-carbaldehyde (**5f**), *N*-tosylindole-3-carbaldehyde (**5g**), chromenecarbaldehyde **5h** and pyrazolecarbaldehyde **5i** also reacted well with **4b** to give the products **6bf**–**6bi** in yields of 65, 90, 92 and 72%, respectively (entries 5–8, Table 4). Reaction of *trans*-cinnamaldehyde (**5j**) with **4b** in $BF_3{\cdot}Et_2O/CH_2Cl_2$ at room temp. afforded **6bj** in 60% yield (entry 9, Table 4). However, an aliphatic aldehyde, heptanal (**5k**), did not participate in the reaction with **4b** even at higher temperatures (entry 10, Table 4). This demonstrates that the developed protocol is suitable only for aromatic aldehydes and a completely electron-rich substrate.

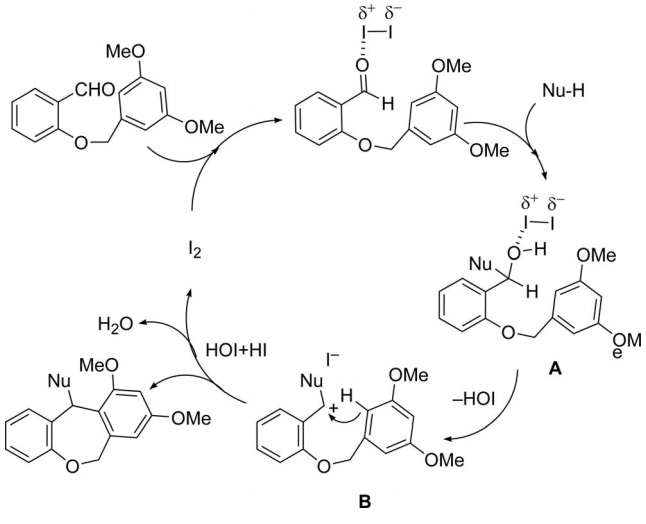
A plausible reaction mechanism is shown in Scheme 3. Mechanistically, it is conceivable that the reaction involves the initial formation of intermediate alcohol **A** by the addition of a nucleophile to the aldehyde and a subsequent intramolecular Friedel–Crafts-type cyclization of **A** via the formation of benzylic carbocation **B** in the presence of an iodine catalyst.[12] The reactions of **1b** with nucleophiles **2a**–**i** provided directly the products **3ba**–**bi** without isolation of any intermediates. However, from the reaction of **1b** with **2i** in $BF_3{\cdot}Et_2O/CH_2Cl_2$, the intermediate **8** was isolated along with **3bi** after 1 h. The intermediate **8** was converted into **3bi** under the same reactions conditions (Scheme 4).[13] The mechanism was further supported by the reaction of **1b** in I_2/CH_3CN in the absence of a nucleophile, which did not proceed to give the expected **7** (Scheme 4).



Scheme 4. Reactions of **1b**.

Conclusions

We have developed a facile method for the synthesis of 11-substituted dibenzoxepine derivatives. The method involves an acid-catalysed tandem nucleophilic addition/Friedel–Crafts-type cyclization reaction. Two different strategies have been demonstrated: 1) the reaction of *O*-(benzyloxy)salicylaldehyde with various nucleophiles under I_2 catalysis and 2) the reaction of *O*-(benzyloxy)phenol with aromatic aldehydes by $BF_3{\cdot}Et_2O$ catalysis. The method requires 10 mol-% of inexpensive I_2 or $BF_3{\cdot}Et_2O$ to obtain the desired products in good yields. Furthermore, the mild reaction conditions and operational simplicity render this approach an interesting method. Although there are a few limitations regarding the substrates, this method opens up a new approach to accessing dibenzoxepine derivatives.



Scheme 3. Proposed mechanism for the iodine-mediated cyclization of **1b**.

Experimental Section

General: ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on 300, 500 or 75 MHz spectrometers at ambient temperature. The chemical shifts (δ) are reported in ppm downfield from TMS as internal standard and signal patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublet; td, triplet of doublet; t, triplet; m, multiplet; br. s, broad singlet. The coupling constants (*J*) are given in Hz. The FTIR spectra were recorded as KBr thin films or neat. For low (MS) and high (HRMS) resolution mass spectrometry, *m*/*z* ratios are reported as atomic mass units. All the reagents and solvents were reagent grade and used without further purification unless specified otherwise. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. Column chromatography was carried out by using silica gel (60–120 mesh) packed in glass columns. All the reactions were performed under nitrogen in flame- or oven-dried glassware with magnetic stirring.

General Procedure for the Preparation of 11-Substituted Dibenzo[*b*,*e*]oxepines 3ba–3bi, 3ca–3cd and 3db: The appropriate nucleophile (1 mmol) was added to a solution of *O*-benzyloxysalicylal-

dehyde **1b**, **1c** or **1d** (1 mmol) in CH_3CN (5 mL), followed by molecular iodine (10 mol-%). The resulting mixture was stirred at room temp. for the given time (Table 2) under nitrogen. After completion of the reaction, the mixture was quenched with water (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (15 mL), dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexanes) to afford the corresponding product.

3-(8,10-Dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-1-methyl-1*H*-indole (3ba): Pale-yellow solid; m.p. 165–166 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3453, 2940, 1605, 1481, 1372, 1104, 933, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.96 (dd, J = 1.5, 7.5 Hz, 1 H, Ar), 6.90–6.72 (m, 4 H, Ar), 6.62–6.49 (m, 3 H, Ar), 6.21 (d, J = 2.0 Hz, 1 H, Ar), 6.11 (d, J = 1.1 Hz, 1 H, Ar), 5.99 (d, J = 2.0 Hz, 1 H, Ar), 5.63 (s, 1 H, CHAr), 5.44 (d, J = 12.6 Hz, 1 H, OCH_2Ar), 4.15 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.64 (s, 3 H, OMe), 3.46 (s, 3 H, OMe), 3.34 (s, 3 H, NMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2, 157.3, 157.1, 137.8, 137.3, 132.9, 128.5, 128.2, 127.3, 126.0, 123.1, 121.2, 120.9, 120.1, 120.0, 119.8, 118.6, 108.9, 105.4, 98.5, 69.7, 55.8, 55.2, 37.9, 32.5 ppm. HRMS (EI): calcd. for $C_{25}H_{23}NNaO_3$ $[M + Na]^+$ 408.1570; found 408.1551.

8,10-Dimethoxy-11-(2,4,6-trimethoxyphenyl)-6,11-dihydrodibenzo-[*b*,*e*]oxepine (3bb): White solid; m.p. 204–205 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3462, 2934, 2842, 1725, 1601, 1149, 948, 635 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.05 (dd, J = 1.7, 8.4 Hz, 1 H, Ar), 6.94–6.87 (m, 1 H, Ar), 6.7 (d, J = 8.4 Hz, 2 H, Ar), 6.23 (d, J = 18 Hz, 2 H, Ar), 6.03 (s, 2 H, Ar), 5.95 (s, 2 H, Ar), 5.63 (d, J = 13 Hz, 1 H, OCH_2Ar), 4.73 (d, J = 13.5 Hz, 1 H, OCH_2Ar), 3.69 (s, 3 H, OMe), 3.67 (s, 3 H, OMe), 3.61 (s, 3 H, OMe), 3.57 (s, 6 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 158.8, 158.5, 158.1, 140.0, 132.4, 131.6, 128.4, 126.5, 121.9, 120.0, 116.2, 103.7, 101.7, 97.9, 91.5, 74.4, 55.1, 55.0, 55.85, 55.6, 36.8 ppm. HRMS (EI): calcd. for $C_{25}H_{27}O_6$ $[M + H]^+$ 423.1802; found 423.1792.

4-(8,10-Dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)phenol (3bc): Pale-yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 3428, 3011, 2943, 1604, 1506, 1363, 1103, 938, 680 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.20–7.08 (m, 2 H, Ar), 6.91–6.75 (m, 4 H, Ar), 6.64–6.56 (m, 2 H, Ar), 6.46 (d, J = 2.3 Hz, 1 H, Ar), 6.34 (d, J = 2.3 Hz, 1 H, Ar), 5.70 (s, 1 H, CHAr), 5.22 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.59 (s, 1 H, OH), 4.46 (d, J = 13.59 Hz, 1 H, OCH_2Ar), 3.88 (s, 3 H, OMe), 3.79 (s, 3 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 157.6, 157.3, 153.5, 138.3, 137.3, 133.7, 128.5, 128.3, 126.9, 123.9, 121.3, 120.4, 114.9, 105.4, 98.5, 70.2, 55.9, 55.3, 43.6 ppm. HRMS (EI): calcd. for $C_{22}H_{21}O_4$ $[M + H]^+$ 349.1434; found 349.1437.

3-(8,10-Dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-1*H*-indole (3bd): Pale-yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 3419, 3009, 2929, 2840, 2100, 1608, 1426, 1051, 934, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.80 (br. s, 1 H, NH), 7.35 (d, J = 7.5 Hz, 1 H, Ar), 7.30 (dd, J = 1.5, 7.5 Hz, 1 H, Ar), 7.21–7.12 (m, 2 H, Ar), 6.97 (t, J = 6.7 Hz, 1 H, Ar), 6.84 (q, J = 7.5 Hz, 4 H, Ar), 6.49 (d, J = 2.3 Hz, 1 H, Ar), 6.47 (s, 1 H, Ar), 6.26 (d, J = 2.2 Hz, 1 H, Ar), 5.91 (s, 1 H, CHAr), 5.68 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.41 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.93 (s, 3 H, OMe), 3.74 (s, 3 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.4, 157.3, 137.9, 136.8, 133.0, 128.3, 127.3, 124.0, 121.8, 121.7, 121.1, 120.2, 119.8, 119.3, 111.0, 105.6, 98.7, 69.2, 55.9, 55.3, 38.0 ppm. HRMS (EI): calcd. for $C_{24}H_{22}NO_3$ $[M + H]^+$ 372.1594; found 372.1575.

3-(8,10-Dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-2-phenyl-1*H*-indole (3be): Pale-yellow solid; m.p. 174–175 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3411, 2925, 2844, 1602, 1321, 1146, 1009, 833, 690 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.13 (s, 1 H, NH), 7.54 (d, J = 7.3 Hz, 2 H, Ar), 7.36 (t, J = 7.3 Hz, 2 H, Ar), 7.24 (t, J = 6.6 Hz, 2 H, Ar), 7.19–7.07 (m, 3 H, Ar), 6.94–6.76 (m, 3 H, Ar), 6.63 (s, 1 H, Ar), 6.50 (d, J = 2.2 Hz, 1 H, Ar), 6.35 (d, J = 2.1 Hz, 1 H, Ar), 5.89 (s, 1 H, CHAr), 5.34 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.42 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.91 (s, 3 H, OMe), 3.79 (s, 3 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 157.6, 157.4, 138.2, 138.1, 137.4, 134.1, 129.1, 128.9, 128.4, 127.5, 126.6, 125.0, 124.8, 122.1, 121.1, 120.3, 119.2, 110.5, 105.6, 99.9, 98.5, 135.2, 132.1, 70.0, 55.3, 44.3, 29.7 ppm. HRMS (EI): calcd. for $C_{30}H_{26}NO_3$ $[M + H]^+$ 448.1907; found 448.1916.

3-(8,10-Dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)pentane-2,4-dione (3bf): White solid; m.p. 121–122 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3440, 3100, 2844, 1727, 1604, 1458, 1360, 1199, 939, 781 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.22 (dd, J = 1.5, 7.4 Hz, 1 H, Ar), 7.16–7.13 (m, 1 H, Ar), 6.96 (d, J = 8.8 Hz, 2 H, Ar), 6.23 (d, J = 2.2 Hz, 1 H, Ar), 6.06 (d, J = 2.2 Hz, 1 H, Ar), 5.53 (d, J = 15.3 Hz, 1 H, OCH_2Ar), 5.23 (d, J = 10.9 Hz, 1 H, OCH_2Ar), 4.90 (s, 1 H, CHAr), 3.80 (s, 3 H, OMe), 3.76 (d, J = 1.5 Hz, 1 H, CHCO), 3.72 (s, 3 H, OMe), 1.98 (s, 3 H, $COCH_3$), 1.93 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.9, 203.3, 159.5, 157.5, 156.9, 138.4, 134.2, 131.0, 128.9, 124.1, 121.2, 117.6, 102.1, 97.0, 73.1, 73.0, 55.5, 55.1, 39.9, 31.3, 29.1 ppm. HRMS (EI): calcd. for $C_{21}H_{22}NaO_5$ $[M + Na]^+$ 377.1359; found 377.1365.

2-(8,10-Dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-3-hydroxycyclohex-2-enone (3bg): Pale-yellow solid; m.p. 183–184 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3136, 2936, 2838, 1645, 1456, 1322, 1016, 778 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.54 (s, 1 H, OH), 7.59 (d, J = 7.5 Hz, 1 H, Ar), 7.24–7.03 (m, 3 H, Ar), 6.32 (s, 1 H, Ar), 6.16 (d, J = 1.5 Hz, 1 H, Ar), 6.01 (s, 1 H, CHAr), 5.31 (d, J = 15.1 Hz, 1 H, OCH_2Ar), 5.06 (d, J = 15.1 Hz, 1 H, OCH_2Ar), 3.75 (s, 6 H, OMe), 2.45–2.15 [m, 4 H, $(COCH_2)_2$], 1.88–1.69 [m, 2 H, $CH_2(CH_2)_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.4, 170.9, 159.4, 158.8, 157.6, 134.8, 132.1, 128.2, 126.1, 120.7, 120.1, 118.5, 101.2, 98.2, 76.7, 55.5, 55.2, 36.7, 35.4, 30.0, 20.5 ppm. HRMS (EI): calcd. for $C_{22}H_{23}O_5$ $[M + H]^+$ 367.1540; found 367.1531.

3-(8,10-Dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-4-hydroxy-2*H*-chromen-2-one (3bh): White solid; m.p. 194–195 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3073, 2946, 1705, 1491, 1326, 1107, 940, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 10.19 (s, 1 H, OH), 7.74 (dd, J = 2.2, 7.5 Hz, 1 H, Ar), 7.69 (dd, J = 1.5, 7.5 Hz, 1 H, Ar), 7.40–7.34 (m, 1 H, Ar), 7.26–7.06 (m, 5 H, Ar), 6.34 (d, J = 3.0 Hz, 1 H, Ar), 6.28 (s, 1 H, CHAr), 6.11 (d, J = 2.3 Hz, 1 H, OCH_2Ar), 5.43 (d, J = 14.4 Hz, 1 H, OCH_2Ar), 5.17 (d, J = 14.4 Hz, 3 H, Ar), 3.79 (s, 3 H, OMe), 3.76 (s, 3 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.6, 159.7, 159.3, 157.6, 152.1, 137.2, 133.8, 131.9, 131.5, 131.2, 129.0, 126.6, 123.5, 123.4, 121.0, 117.1, 116.9, 116.0, 109.7, 101.6, 98.2, 76.9, 55.8, 55.3, 38.4 ppm. HRMS (EI): calcd. for $C_{25}H_{21}O_6$ $[M + H]^+$ 417.1333; found 417.1317.

11-Allyl-8,10-dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepine (3bi): Yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 3452, 2945, 2838, 1726, 1605, 1162, 952, 678 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.10 (d, J = 7.5 Hz, 2 H, Ar), 6.93 (s, 1 H, Ar), 6.91 (s, 1 H, Ar), 6.31 (d, J = 2.2 Hz, 1 H, Ar), 6.12 (d, J = 2.2 Hz, 1 H, Ar), 5.69–5.53 (m, 1 H, $CH=CH_2$), 5.39 (d, J = 15.0 Hz, 1 H, OCH_2Ar), 4.86 (d, J = 15.0 Hz, 1 H, OCH_2Ar), 4.83–4.76 (m, 2 H, $CH_2=CH$), 4.41 (t, J = 7.5 Hz, 1 H, CH), 3.84 (s, 3 H, OMe), 3.70 (s, 3 H, OMe), 2.86–2.73 [m, 1 H, $CH_2(CH=CH_2)$], 2.66–2.53 [m, 1 H, $CH_2(CH=CH_2)$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 157.44, 138.2, 137.3, 133.7, 131.8, 127.9, 123.0, 120.7, 115.4, 104.8, 102.7, 97.6, 73.1, 55.7, 55.2, 43.2, 41.5, 38.8 ppm. HRMS (EI): calcd. for $C_{19}H_{21}O_3$ $[M + H]^+$ 297.1485; found 297.1471.

3-(2-Bromo-8,10-dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-1-methyl-1*H*-indole (3ca): Yellow solid; m.p. 121–124 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3436, 2926, 1608, 1479, 1205, 1012, 719 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40 (d, J = 2.7 Hz, 1 H, Ar), 7.25–7.16 (m, 2 H, Ar), 7.12–7.07 (m, 2 H, Ar), 6.89 (t, J = 7.3 Hz, 1 H, Ar), 6.74 (d, J = 8.2 Hz, 1 H, Ar), 6.55 (d, J = 1.8 Hz, 1 H, Ar), 6.45 (s, 1 H, Ar), 6.30 (d, J = 2.7 Hz, 1 H, Ar), 5.90 (s, 1 H, CHAr), 5.73 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.45 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.97 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.69 (s, 3 H, NCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.5, 157.1, 156.5, 137.4, 135.1, 131.0, 129.2, 128.5, 125.9, 122.5, 122.0, 121.4, 119.8, 119.4, 118.8, 112.7, 109.0, 105.7, 98.7, 69.8, 55.8, 55.3, 37.6, 32.6 ppm. MS (ESI): m/z = 487 $[M + Na]^+$.

2-Bromo-8,10-dimethoxy-11-(2,4,6-trimethoxyphenyl)-6,11-dihydrodibenzo[*b*,*e*]oxepine (3cb): White solid; m.p. 197–199 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3475, 2937, 2854, 1732, 1612, 1155, 965, 637 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.25 (s, 1 H, Ar), 7.07 (dd, J = 1.5, 8.4 Hz, 1 H, Ar), 6.70 (d, J = 8.5 Hz, 1 H, Ar), 6.26 (s, 1 H, Ar), 6.20 (s, 1 H, Ar), 6.02 (s, 3 H, CHAr), 5.63 (d, J = 13.1 Hz, 1 H, OCH_2Ar), 4.75 (d, J = 13.1 Hz, 1 H, OCH_2Ar), 3.75 (s, 3 H, OMe), 3.73 (s, 3 H, OMe), 3.69 (s, 3 H, OMe), 3.62 (s, 6 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 158.8, 158.4, 158.4, 157.7, 139.4, 134.6, 134.2, 129.5, 121.8, 121.4, 115.3, 114.3, 103.8, 98.0, 91.6, 55.9, 55.7, 55.2, 55.1, 36.7, 29.7 ppm. HRMS (EI): calcd. for $C_{23}H_{27}BrNaO_6$ $[M + Na]^+$ 503.0866; found 503.0897.

4-(2-Bromo-8,10-dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-phenol (3cc): Pale-yellow liquid. IR (KBr): $\tilde{\nu}_{max}$ = 3520, 3014, 2950, 1607, 1510, 1367, 1109, 944, 685 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.33 (d, J = 1.8 Hz, 1 H, Ar), 7.25–7.21 (m, 1 H, Ar), 6.78 (d, J = 8.2 Hz, 1 H, Ar), 6.73 (d, J = 9.2 Hz, 1 H, Ar), 6.62 (d, J = 8.3 Hz, 2 H, Ar), 6.49 (d, J = 1.8 Hz, 1 H, Ar), 6.33 (d, J = 1.8 Hz, 1 H, Ar), 5.68 (s, 1 H, CHAr), 5.35 (s, 1 H, OH), 5.21 (d, J = 12.9 Hz, 1 H, OCH_2Ar), 4.46 (d, J = 12.9 Hz, 1 H, OCH_2Ar), 3.89 (s, 3 H, OMe), 3.80 (s, 3 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 157.6, 156.4, 153.7, 136.9, 135.7, 131.4, 128.8, 128.3, 123.3, 122.3, 115.0, 113.2, 105.6, 98.62, 70.2, 50.0, 55.4, 43.3 ppm. HRMS (EI): calcd. for $C_{20}H_{21}BrNaO_4$ $[M + Na]^+$ 427.0515; found 427.0496.

3-(2-Bromo-8,10-dimethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-1*H*-indole (3cd): Pale-yellow solid; m.p. 201–202 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3420, 3100, 2940, 2842, 2110, 1610, 1488, 1321, 1051, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.86 (br. s, 1 H, NH), 7.38 (s, 1 H, Ar), 7.19 (d, J = 9.2 Hz, 1 H, Ar), 7.14 (d, J = 7.3 Hz, 1 H, Ar), 7.10–6.98 (m, 2 H, Ar), 6.86 (t, J = 7.3 Hz, 1 H, Ar), 6.70 (d, J = 9.2 Hz, 1 H, Ar), 6.50 (d, J = 12.9 Hz, 1 H, Ar), 6.25 (s, 1 H, Ar), 5.87 (s, 1 H, CHAr), 5.65 (d, J = 12.9 Hz, 1 H, OCH_2Ar), 4.39 (d, J = 11.9 Hz, 1 H, OCH_2Ar), 3.95 (s, 3 H, OMe), 3.74 (s, 3 H, OCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.4, 157.3, 137.9, 136.8, 133.0, 128.3, 127.3, 124.0, 121.8, 121.7, 121.2, 120.2, 119.8, 119.3, 111.0, 105.6, 98.8, 69.8, 55.9, 55.3, 39.0 ppm. HRMS (EI): calcd. for $C_{24}H_{21}BrNO_3$ $[M + H]^+$ 450.0699; found 450.0697.

8,10-Dimethoxy-11-(2,4,6-trimethoxyphenyl)dibenzo[*b*,*e*]oxepin-6(11*H*)-one (3db): White solid; m.p. 147–148 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3461, 2936, 2840, 1727, 1365, 1203, 1053, 827, 755 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, J = 15 Hz, 1 H, Ar), 7.45 (d, J = 7.5 Hz, 1 H, Ar), 7.17–6.95 (m, 4 H, Ar), 6.52 (d, J = 2.2 Hz, 1 H, Ar), 6.19 (s, 1 H, CHAr), 6.0 (s, 2 H, OCH_2Ar), 3.81 (s, 6 H, OMe), 3.72 (s, 3 H, OMe), 3.63 (s, 6 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 158.4, 157.0, 157.7, 139.6, 132.0, 131.2, 127.9, 126.0, 121.5, 119.6, 115.8, 103.3, 97.5, 91.1, 55.4, 55.2, 54.7, 54.6, 36.3 ppm. HRMS (EI): calcd. for $C_{25}H_{25}O_7$ $[M + H]^+$ 437.1595; found 437.1611.

General Procedure for the Preparation of 11-Substituted Dibenzo-[*b*,*e*]oxepines 6ba–bj: The appropriate aromatic aldehyde (1 mmol) was added to a solution of *O*-benzyloxyphenol **4b** (1 mmol) in CH_2Cl_2 (5 mL) followed by $BF_3{\cdot}Et_2O$ (10 mol-%). The resulting mixture was stirred at room temp. for a given time (Table 4). After completion of the reaction, the mixture was quenched with water (5 mL) and extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (15 mL), dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexanes) to afford the corresponding product.

1,3,8,10-Tetramethoxy-11-phenyl-6,11-dihydrodibenzo[*b*,*e*]oxepine (6ba): White solid; m.p. 176–178 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2928, 2846, 1736, 1610, 1461, 1154, 1108, 736, 833 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.12 (t, J = 7.2 Hz, 2 H, Ar), 7.05 (d, J = 7.2 Hz, 1 H, Ar), 6.90 (d, J = 7.9 Hz, 2 H, Ar), 6.47 (d, J = 2.2 MHz, 1 H, Ar), 6.33 (s, 1 H, CHAr), 6.32 (d, J = 2.2 Hz, 1 H, Ar), 6.10 (d, J = 2.6 Hz, 1 H, Ar), 5.98 (d, J = 2.4 Hz, 1 H, Ar), 5.14 (d, J = 12.6 Hz, 1 H, OCH_2Ar), 4.40 (d, J = 12.6 Hz, 1 H, OCH_2Ar), 3.89 (s, 3 H, OMe), 3.79 (s, 6 H, OMe), 3.74 (s, 3 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.6, 159.4, 158.8, 157.9, 146.1, 137.8, 127.8, 127.0, 125.2, 124.5, 108.7, 105.2, 99.9, 98.5, 96.3, 93.7, 93.2, 92.5, 70.1, 56.0, 55.9, 55.3, 55.1, 33.9 ppm. HRMS (EI): calcd. for $C_{24}H_{24}O_5$ $[M + H]^+$ 393.1697; found 393.1708.

1,3,8,10-Tetramethoxy-11-(naphthalen-1-yl)-6,11-dihydrodibenzo-[*b*,*e*]oxepine (6bb): Pale-yellow solid; m.p. 204–207 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2926, 2850, 1733, 1606, 1457, 1143, 1104, 783, 828 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.37 (t, J = 5.3 Hz, 1 H, Ar), 7.73 (t, J = 5.3 Hz, 1 H, Ar), 7.61 (d, J = 8.3 Hz, 1 H, Ar), 7.37–7.27 (m, 4 H, Ar), 6.87 (s, 1 H, CHAr), 6.44 (d, J = 2.2 Hz, 1 H, Ar), 6.19 (d, J = 3.0 Hz, 1 H, Ar), 6.12 (d, J = 3.0 Hz, 1 H, Ar), 6.05 (d, J = 2.2 Hz, 1 H, Ar), 5.60 (d, J = 13.5 Hz, 1 H, OCH_2Ar), 4.51 (d, J = 13.5 Hz, 1 H, OCH_2Ar), 3.92 (s, 3 H, OMe), 3.81 (s, 3 H, OMe), 3.74 (s, 3 H, OMe), 3.72 (s, 3 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.8, 159.2, 159.1, 157.9, 157.2, 141.5, 138.2, 134.0, 131.8, 128.4, 127.3, 126.8, 125.2, 125.0, 124.9, 124.8, 123.3, 112.4, 104.3, 98.7, 97.2, 93.5, 70.7, 56.2, 56.1, 55.6, 55.1, 32.6 ppm. HRMS (EI): calcd. for $C_{28}H_{26}O_5$ $[M + H]^+$ 443.1853; found 443.1838.

4-(1,3,8,10-Tetramethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)phenol (6bc): White solid; m.p. 218–221 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3397, 2936, 2843 (s), 2359, 1734, 1610, 1206, 1099, 833 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.76 (d, J = 8.4 Hz, 2 H, Ar), 6.58 (d, J = 8.4 Hz, 2 H, Ar), 6.46 (d, J = 2.2 Hz, 1 H, Ar), 6.32 (d, J = 2.2 Hz, 2 H, Ar), 6.23 (s, 1 H, CHAr), 6.09 (d, J = 2.5 Hz, 1 H, Ar), 5.98 (d, J = 2.2 Hz, 1 H, Ar), 5.17 (d, J = 12.6 Hz, 1 H, OCH_2Ar), 4.41 (d, J = 12.6 Hz, 1 H, OCH_2Ar), 3.88 (s, 3 H, OMe), 3.79 (s, 6 H, OMe), 3.74 (s, 3 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.5, 159.3, 159.2, 158.8, 157.8, 153.3, 138.2, 137.8, 128.1, 124.5, 114.7, 109.0, 105.2, 98.5, 96.3, 92.5, 70.1, 56.1, 55.9, 55.3, 55.1, 33.2 ppm. HRMS (EI): calcd. for $C_{24}H_{24}O_6$ $[M + H]^+$ 409.1646; found 409.1656.

11-(3,5-Dimethoxyphenyl)-1,3,8,10-tetramethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepine (6bd): White solid; m.p. 159–162 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2998, 2959, 2931, 2839, 1605, 1458, 1151, 710, 833 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.46 (s, 1 H, Ar), 6.33 (d, J = 2.1 Hz, 1 H, Ar), 6.25 (s, 1 H, CHAr), 6.14 (s, 1 H, Ar), 6.09 (d, J = 2.2 Hz, 1 H, Ar), 6.05 (s, 2 H, Ar), 5.97 (d, J = 2.2 Hz, 1 H, Ar), 5.23 (d, J = 13.2 Hz, 1 H, OCH_2Ar), 4.42 (d, J = 13.2 Hz, 1 H, OCH_2Ar), 3.88 (s, 3 H, OMe), 3.79 (s, 6 H, OMe), 3.73 (s, 3 H, OMe), 3.64 (s, 6 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 160.4, 159.7, 159.4, 158.7, 157.8, 149.0, 137.8, 124.2, 108.4, 106.0, 105.3, 98.6,

96.5, 96.3, 92.5, 70.1, 56.1, 56.0, 55.3, 55.0 ppm. HRMS (EI): calcd. for $C_{26}H_{28}O_7$ [M + H]$^+$ 453.1908; found 453.1893.

1,3,8,10-Tetramethoxy-11-(4-nitrophenyl)-6,11-dihydrodibenzo[*b*,*e*]-oxepine (6be): Viscous liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2938, 2842, 1727, 1609, 1345, 1269, 1148, 1106, 735, 832 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.02 (d, J = 9.0 Hz, 2 H, Ar), 7.12 (d, J = 9.0 Hz, 2 H, Ar), 6.48 (d, J = 2.2 Hz, 1 H, Ar), 6.35 (s, 1 H, CHAr), 6.30 (d, J = 2.2 Hz, 1 H, Ar), 6.14 (d, J = 2.2 Hz, 1 H, Ar), 6.03 (d, J = 2.2 Hz, 1 H, Ar), 5.02 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.51 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.90 (s, 3 H, OMe), 3.81 (s, 6 H, OMe), 3.75 (s, 3 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 160.1, 159.7, 159.0, 158.9, 157.8, 154.2, 145.7, 137.8, 127.9, 123.1, 122.2, 108.8, 104.7, 98.4, 96.7, 93.0, 70.7, 56.04, 56.00, 55.3, 55.2, 34.5 ppm. HRMS (EI): calcd. for $C_{24}H_{23}NO_7$ [M + H]$^+$ 438.1547; found 438.1557.

1,3,8,10-Tetramethoxy-11-(thiophen-2-yl)-6,11-dihydrodibenzo[*b*,*e*]-oxepine (6bf): Pale-yellow solid; m.p. 185–188 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2929, 2843, 1734, 1608, 1148, 1108, 1056, 814, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.97 (d, J = 5.3 Hz, 1 H, Ar), 6.78–6.76 (m, 1 H, Ar), 6.45 (d, J = 2.3 Hz, 1 H, Ar), 6.41 (s, 1 H, CHAr), 6.39 (t, J = 1.5 Hz, 1 H, Ar), 6.36 (d, J = 2.3 Hz, 1 H, Ar), 6.10 (d, J = 2.3 Hz, 1 H, Ar), 5.97 (d, J = 3.0 Hz, 1 H, Ar), 5.36 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.50 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.89 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 3.81 (s, 3 H, OMe), 3.74 (s, 3 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.8, 159.7, 159.2, 158.9, 157.5, 151.8, 138.5, 126.3, 123.5, 123.1, 123.6, 109.8, 105.3, 98.5, 96.4, 92.7, 70.6, 56.1, 55.3, 55.2, 31.2 ppm. HRMS (EI): calcd. for $C_{22}H_{22}O_5S$ [M + H]$^+$ 399.1261; found 399.1267.

3-(1,3,8,10-Tetramethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-1-tosyl-1*H*-indole (6bg): White solid; m.p. 204–207 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2928, 2853, 1731, 1609, 1173, 1144, 1109, 810, 740 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.89 (d, J = 7.7 Hz, 1 H, Ar), 7.63 (d, J = 8.7 Hz, 2 H, Ar), 7.17 (m, 3 H, Ar), 7.10 (d, J = 7.7 Hz, 1 H, Ar), 7.01 (t, J = 7.7 Hz, 1 H, Ar), 6.96 (s, 1 H, Ar), 6.48 (d, J = 1.9 Hz, 1 H, Ar), 6.35 (s, 1 H, CHAr), 6.26 (d, J = 1.9 Hz, 1 H, Ar), 6.14 (d, J = 1.9 Hz, 1 H, Ar), 6.05 (d, J = 1.9 Hz, 1 H, Ar), 5.49 (d, J = 12.6 Hz, 1 H, OCH_2Ar), 4.43 (d, J = 12.6 Hz, 1 H, OCH_2Ar), 3.93 (s, 3 H, OMe), 3.80 (s, 3 H, OMe), 3.78 (s, 6 H, OMe), 2.35 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.7, 159.4, 159.0, 158.5, 157.3, 144.4, 138.4, 135.9, 135.0, 129.9, 129.5, 128.6, 126.6, 125.0, 124.1, 123.0, 121.4, 120.5, 113.6, 108.8, 104.9, 98.6, 96.7, 92.8, 69.8, 55.9, 55.2, 55.1, 27.4, 21.4 ppm. HRMS (EI): calcd. for $C_{33}H_{31}NO_7S$ [M + H]$^+$ 586.1894; found 586.1869.

3-(1,3,8,10-Tetramethoxy-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-yl)-4*H*-chromen-4-one (6bh): White solid; m.p. 213–216 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3081, 2927, 2843, 1728, 1649, 1609, 1144, 1105, 831, 752 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.12 (dd, J = 8.3, 1.5 Hz, 1 H, Ar), 7.56 (d, J = 1.5 Hz, 1 H, Ar), 7.51 (dd, J = 6.7, 1.5 Hz, 1 H, Ar), 7.28 (dd, J = 16.6, 8.3 Hz, 1 H, Ar), 6.40 (d, J = 2.3 Hz, 1 H, Ar), 6.33 (d, J = 1.5 Hz, 1 H, Ar), 6.17 (d, J = 2.2 Hz, 1 H, Ar), 6.15 (d, J = 3.0 Hz, 1 H, CHAr), 6.04 (d, J = 2.3 Hz, 1 H, Ar), 5.51 (d, J = 14.3 Hz, 1 H, OCH_2Ar), 4.74 (d, J = 14.3 Hz, 1 H, OCH_2Ar), 3.90 (s, 3 H, OMe), 3.89 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 3.72 (s, 3 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 176.5, 159.9, 159.6, 159.2, 158.7, 158.4, 155.9, 154.4, 138.4, 132.7, 127.7, 126.0, 124.3, 124.1, 119.0, 117.6, 111.3, 103.0, 98.1, 97.2, 94.0, 71.7, 56.1, 56.0, 55.1, 27.7 ppm. HRMS (EI): calcd. for $C_{27}H_{24}O_7$ [M + H]$^+$ 461.1595; found 461.1603.

3-Methyl-1-phenyl-4-(1,3,8,10-tetramethoxy-6,11-dihydrodibenzo-[*b*,*e*]oxepin-11-yl)-1*H*-pyrazole (6bi): White solid; m.p. 106–109 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2927, 2853, 1727, 1606, 1146, 1107, 828, 759 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.55–7.50 (m, 2 H, Ar), 7.34–7.26 (m, 3 H, Ar), 7.30 (s, 1 H, Ar), 7.15–7.05 (m, 1 H, Ar), 6.40 (d, J = 3.0 Hz, 1 H, Ar), 6.28 (d, J = 3.0 Hz, 1 H, Ar), 6.13 (s, 1 H, CHAr), 6.10 (d, J = 2.3 Hz, 1 H, Ar), 6.02 (d, J = 2.3 Hz, 1 H, Ar), 5.56 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.59 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.89 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.74 (s, 3 H, OMe),1.96 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.6, 159.2, 159.1, 158.5, 157.6, 148.0, 140.1, 138.1, 129.0, 127.0, 126.8, 125.2, 122.1, 118.2, 111.0, 104.3, 98.1, 96.8, 93.0, 70.8, 56.0, 55.7, 55.2, 55.1, 25.9, 12.1 ppm. HRMS (EI): calcd. for $C_{28}H_{28}N_2O_5$ [M + H]$^+$ 473.2071; found 473.2081.

(*E*)-1,3,8,10-Tetramethoxy-11-styryl-6,11-dihydrodibenzo[*b*,*e*]-oxepine (6bj): Viscous liquid. IR (KBr): $\tilde{\nu}_{max}$ = 2931, 2844, 1611, 1147, 1107, 768, 821 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.23 (d, J = 6.8 Hz, 2 H, Ar), 7.16 (t, J = 7.5 Hz, 2 H, Ar), 7.06 (t, J = 6.8 Hz, 1 H, Ar), 6.45 (dd, J = 4.5, 15.8 Hz, 2 H, Ar), 6.33 (d, J = 6.8 Hz, 1 H, Ar), 6.10 (br. s, 1 H, Ar), 5.99 (br. s, 2 H, CH), 5.79 (br. s, 1 H, CHAr), 5.57 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 4.59 (d, J = 12.8 Hz, 1 H, OCH_2Ar), 3.86 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.80 (s, 3 H, OMe), 3.73 (s, 3 H, OMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.3, 159.3, 159.1, 157.6, 138.5, 134.8, 137.6, 126.1, 126.6, 127.7, 128.2, 127.0, 127.8, 108.7, 104.8, 98.6, 96.2, 92.7, 70.9, 56.0, 55.9, 55.3, 55.2, 33.2 ppm. HRMS (EI): calcd. for $C_{26}H_{26}O_5$ [M + H]$^+$ 419.1853; found 419.1862.

1-[2-(3,5-Dimethoxybenzyloxy)phenyl]but-3-en-1-ol (8): Pale-yellow liquid. IR (KBr): $\tilde{\nu}_{max}$ = 3448, 3070, 2934, 2842, 1720, 1603, 1487, 1367, 1287 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (dd, J = 7.3, 1.1 Hz, 1 H, Ar), 7.16 (dt, J = 8.1, 1.5 Hz, 1 H, Ar), 6.93 (t, J = 7.3 Hz, 1 H, Ar), 6.85 (d, J = 8.1 Hz, 1 H, Ar), 6.50 (d, J = 2.0 Hz, 1 H, Ar), 6.34 (t, J = 2.0 Hz, 1 H, Ar), 5.89–5.74 (m, 1 H, C*H*=CH_2), 5.14–4.96 (m, 5 H, O*C*H_2Ar, CH_2=CH, ArC*H*OH), 3.77 (s, 6 H, 2 OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.7, 158.3, 157.8, 138.2, 137.2, 133.7, 131.8, 127.9, 122.9, 121.8, 120.7, 115.3, 102.8, 97.6, 73.1, 55.7, 55.2, 43.2, 41.5 ppm. MS (ESI): m/z = 315 [M + H]$^+$.

Supporting Information (see footnote on the first page of this article): Experimental procedures, spectroscopic data for **1b**–**d**, **3a**, **4a** and **4b** and ^{1}H and ^{13}C NMR spectra for all the reaction products.

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[12] In the control experiment of **1b** with **2b** using in situ generated HI, no conversion was observed. HI was generated by the addition of TMSCl and water to a solution of NaI in CH_3CN, see: S. Irifune, T. Kibayashi, Y. Ishii, M. Ogawa, *Synthesis* **1988**, 366–369.

[13] Triarylmethane **3a** was obtained only in the case of **1a**, whereas the electron-rich substrate **1b** provided dibenzoxapine **3aa** (Table 1). This clearly supports the proposed mechanism, which differs from the concept of xanthene synthesis, see ref.[9]

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