Palladium(0)-Catalyzed Intramolecular Heck Reaction: A Resourceful Route for the Synthesis of Naphthoxepine and Naphthoxocine Derivatives

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Abstract: The synthesis of oxocines and oxepines is difficult. Two efficient protocols have been developed for the construction of naphthoxepine and naphthoxocine derivatives by sequential Wittig olefination and intramolecular Heck reaction.

Key words: Wittig olefination, oxepines, oxocines, Heck cyclization, palladium catalysis

A number of medium-sized heterocyclic rings form part of the structures of a range of biologically active natural products[1] and medicinally important compounds.[2] Owing to this and other reasons, over the last few years several methodologies have been developed[3] for the construction of such ring systems. Enthalpic and entropic factors[4] have made the construction of medium-sized rings much more difficult. Generally, most of the classical cyclization strategies are often hampered by entropic factors and transannular interactions.[5] In particular, relatively fewer methods based on cyclization or cycloaddition have been implemented[6] for the synthesis of medium-ring heterocyclic compounds from acyclic starting materials, although these have been extensively used for the synthesis of regular heterocyclic systems. Therefore, the development of new synthetic protocols for the synthesis of medium-ring heterocyclic compounds remains a challenge.

Oxepines and oxocines are important structural units present in numerous biologically active molecules and have attracted considerable attention during the last few years. Beside this, benzo-fused oxepine and oxocine derivatives belong to a class of medicinally important compounds. These exhibit antianaphylactic,[7] oral hypotensive,[8] and antiulcer properties. Moreover, benzoxepine and -oxocine moieties are prevalent in many important bioactive natural products such as radulanin,[9] helianuols,[10] and pterulone,[11] as well as in some modern pharmaceuticals with lipoxegenase inhibition activity.[12] Therefore, the synthesis of these units carrying different functionalities is important. Interestingly, despite their broad spectrum of biological activity, benzo- and dibenzo-fused oxepine and oxocine derivatives are not sufficiently investigated, and one possible reason is the lack of simple and straightforward synthetic procedures. Figure 1 represents some naturally occurring oxepine and oxocine derivatives.

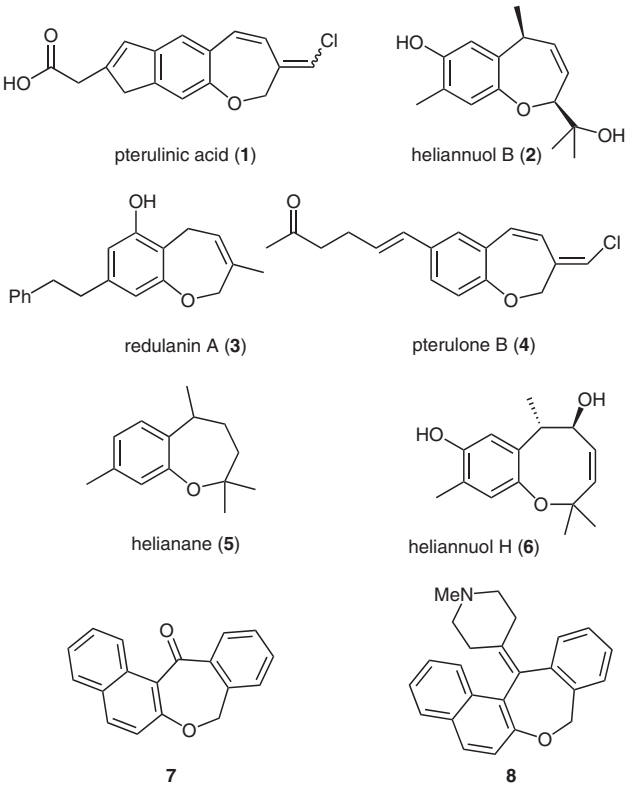

Figure 1 Some of the important naturally occurring bioactive oxocines and oxepines

Recently, we attempted[13] to synthesize compounds **7** and **8** (Figure 1) by the application of the intramolecular Heck reaction. For this purpose, we had chosen precursor **9a** with a vinyl group attached to the aromatic moiety, with the expectation to achieve the *exo-trig* mode of Heck cyclization. However, 8-*endo-trig* cyclization occurred to provide an efficient protocol for the construction of the eight-membered ring system instead of the expected 7-*exo-trig* cyclization by the intramolecular Heck reaction from the vinylic precursors (Scheme 1).

These results encouraged us to continue further investigation to achieve a protocol for the preparation of the desired products **7** and **8** via the *exo-trig* mode of cyclization. Herein, we report our results.

It is remarkable to note that naphthoxepine derivatives such as **7** and **8**[2] (Figure 1) are used as antipsychotic drugs

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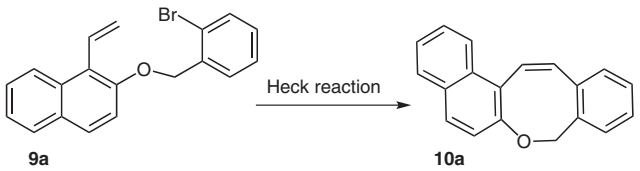


Scheme 1 Synthesis of oxocine via intramolecular Heck reaction

essentially free of extrapyramidal symptoms and can be administered in nontoxic effective quantities of active ingredients to animals.

The synthetic procedure[3] for compounds **7** and **8** is quite complicated. They were synthesized from a complex starting material, 2-(2-carboxybenzyloxy)naphthalene, and a number of reaction sequences were carried out to furnish compounds **7** and **8**.

The retrosynthetic analysis of compound **7** is summarized in Scheme 2. The carbonyl functionality of **7** could arise from simple ozonolysis or periodic acid oxidation of the corresponding *exo*-methylene function. Construction of the seven-membered ring may be accomplished by intramolecular Heck reaction via an *exo-trig* mode of cyclization. The vinyl fragment may be incorporated by Wittig olefination from the corresponding aldehydic compound. This compound may be prepared by simple benzylation of 1-formyl-2-naphthol. Naphthol is easily formylated by various reported protocols.

With our interest in synthesizing medium-sized heterocyclic compounds,[14] we have devised an approach for the construction of the important oxepine and oxocine derivatives employing the Wittig reaction followed by a regioselective intramolecular Heck reaction. We have envisioned that this route would not only lead to the naphthoxepine and naphthoxocine derivatives, but also to a variety of new analogues possessing modifications around the aryl ring.

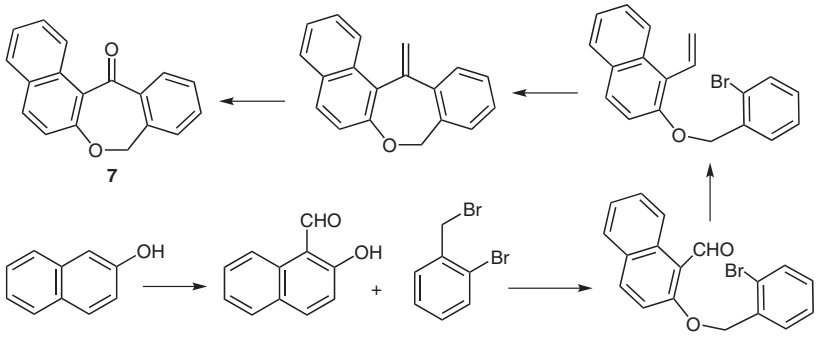
The synthesis of heterocyclic compounds by the application of a palladium-catalyzed intramolecular Heck reaction has been extensively studied in our laboratory during the last few years.[15] A thorough search of the literature revealed that in the case of small- to medium-ring syntheses, the aryl–palladium complex follows an *exo* mode of cyclization, whereas in the case of large-ring syntheses (~20), the *endo* mode becomes favorable.[16] Moreover, recently it has been reported[17] that in the case of highly activated double bonds, i.e., the Michael acceptor, the ring formation become possible through the *endo* mode of cyclization. All these observations encouraged us to carry out the palladium-catalyzed cyclization protocol for synthesizing seven-membered oxepin derivatives, more precisely compounds **7** and **8** (Figure 1).

The required Heck precursors **9a–j** for our investigation were synthesized in 75–95% yields by Wittig reactions of compounds **14a–j** with methyltriphenylphosphonium iodide in anhydrous tetrahydrofuran in the presence of *n*-butyllithium at 0 °C to room temperature for about one hour (Scheme 3). Compounds **14a–j**, in turn, were prepared in almost quantitative yields by the reactions of 1-formyl-2-naphthol (**12a**) or 2-formylphenols **12b–f** with either 2-bromobenzyl bromide (**13a**) or 2-bromo-5-methoxybenzyl bromide (**13b**) in anhydrous acetone in the presence of anhydrous potassium carbonate and a small amount of sodium iodide[18] (Scheme 3). 1-Formyl-2-naphthol (**12a**) was prepared by our recently developed protocol.[13]

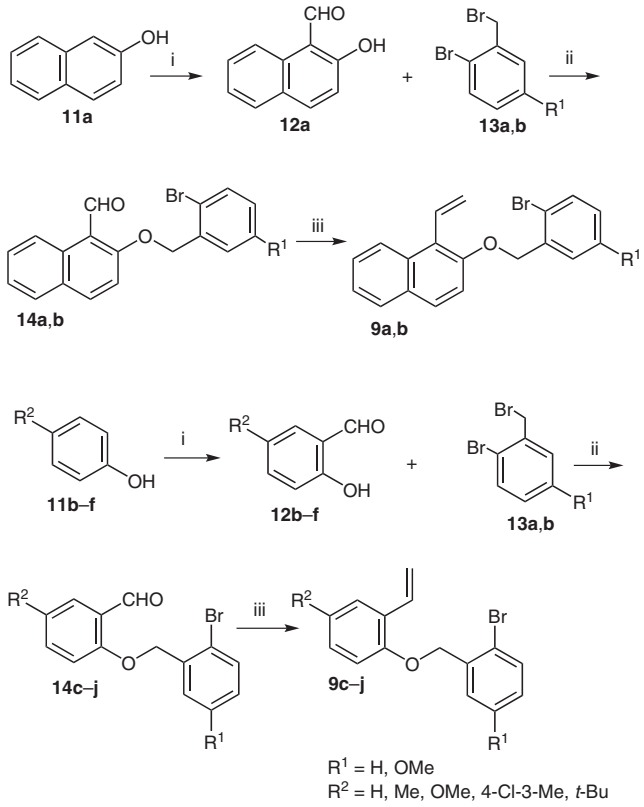
When the intramolecular Heck reaction was performed with the precursor **9b** in the presence of palladium(II) acetate as catalyst, potassium acetate as base, tetrabutylammonium bromide as additive,[19] and in anhydrous *N*,*N*-dimethylformamide as solvent at 100 °C for 3.5 hours under a nitrogen atmosphere, to our utter frustration only eight-membered naphthoxocine derivative **10b** was formed exclusively (67%) without even a trace of the desired seven-membered naphthoxepine derivative **15b** of the corresponding biaryl product **16** (Scheme 4).

Therefore, the reaction conditions were optimized by changing the solvent, the base, and the temperature, and it was found that in all the cases either the yield of the oxocine derivative decreased or the starting material remained completely unchanged. Changing the catalyst did not cause any significant change in the outcome of the reaction. The results are presented in Table 1.

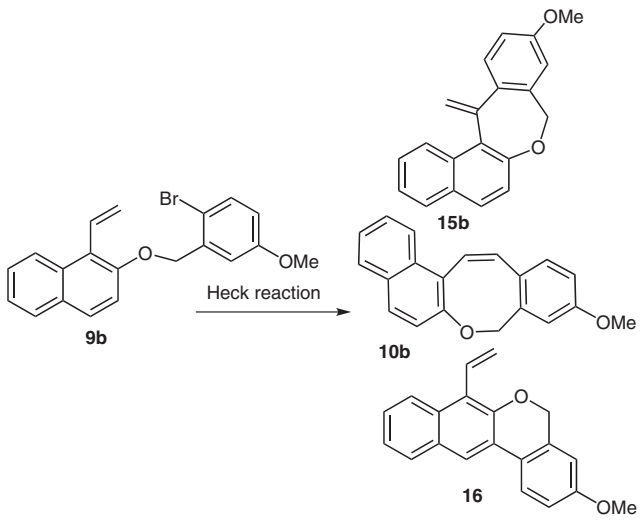
Moreover, we recently reported[20] the synthesis of different oxathiocine derivatives starting from **17** containing the vinylic counterpart, and, again, only eight-membered oxathiocine derivatives such as **18** were isolated in good to excellent yields through *endo* attack at the double bond (Scheme 5).



Scheme 2 Retrosynthetic analysis of compound **7**



Scheme 3 *Reagents and conditions*: (i) aq NaOH, $CHCl_3$, reflux, 4 h; (ii) acetone, K_2CO_3, NaI, 3–4 h; (iii) $MePPh_3I$, *n*-BuLi, THF, 0 °C to r.t.



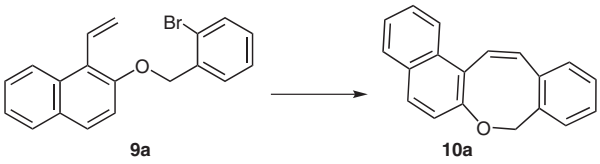
Scheme 4 Intramolecular Heck reaction of **9b**

All these failures inspired us to make an all-out effort to construct the desired seven-membered naphthoxepine **7** by a thorough and constant experimental manipulation.

When the Heck precursor **9a** was allowed to react with 20 mol% tetrakis(triphenylphosphine)palladium as catalyst and anhydrous triethylamine as base in refluxing acetonitrile for 24 hours, the required seven-membered naphthoxepine **15a** was isolated in moderate yields (65%) along with the contamination of the eight-membered naphthoxocine derivative **10a** in 13% yield (Table 2). This observation led us to search for optimized conditions for the formation of the desired compound **15a**. It was found that changing the base to potassium acetate or cesium carbonate either increases the amount of **15a** with almost disappearance of **10a**, or no reaction occurred. On the other hand, changing the solvent to *N*,*N*-dimethylformamide or dimethylacetamide (DMA) resulted in almost all the starting material remaining unchanged, with the formation of a trace amount of **10a**. The amount of catalyst played a crucial role in our investigation. A 5 mol% of tetrakis(triphenylphosphine)palladium was found to be ineffective for the reaction, whereas 20 mol% tetrakis(triphenylphosphine)palladium yielded product **15a** in satisfactory yield. On the basis of our observation, the optimized conditions for the reaction consist of the use of tetrakis(triphenylphosphine)palladium and triethylamine in acetonitrile at reflux for 24 hours, and the results are summarized in Table 2.

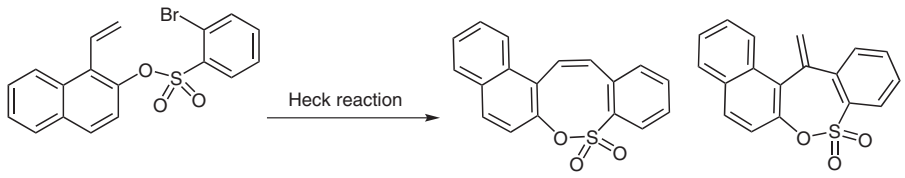
Similarly, all the Heck precursors **9b–j** were treated under the optimized conditions, and the results are summarized in Table 3.

Table 1 Optimization of the Conditions for the Heck Reaction[a]



Entry	Catalyst	Base	Solvent	Yield (%)
1[b]	**$Pd(OAc)_2$**	**KOAc**	**DMF**	**86**
2	$Pd(OAc)_2$	Et_3N	DMF	<5
3	$Pd(OAc)_2$	K_2CO_3	DMF	63
4	$Pd(OAc)_2$	Ag_2CO_3	DMF	NR[c]
5	$Pd(OAc)_2$	Cs_2CO_3	DMF	NR[c]
6[b]	$Pd(PPh_3)_4$	KOAc	DMF	43
7[b]	$Pd(PPh_3)_2Cl_2$	KOAc	DMF	21
8[b]	$PdCl_2$	KOAc	DMF	36
9	$Pd(OAc)_2$	KOAc	DMF	NR[c]
10	$Pd(OAc)_2$	Et_3N	Et_3N	NR[c]
11	$Pd(OAc)_2$	Et_3N	MeCN	NR[c]
12	$Pd(OAc)_2$	Et_3N	dioxane	<5
13	$Pd(OAc)_2$	KOAc	dioxane	<5

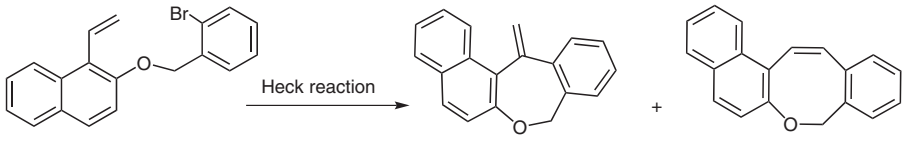
[a] Reagents and conditions: **9a** (1 equiv), base (2.75 equiv), cat. (10 mol%), solvent, 100 °C, 4 h.
[b] In these cases, TBAB was used as additive.
[c] NR = no reaction.



17 **18** observed **19** not observed

Scheme 5 Synthesis of oxathiocine derivatives

Table 2 Screening of the Heck Conditions



9a **15a** (major) **10a** (minor)

Entry	Amount $Pd(PPh_3)_4$ (mol%)	Base	Solvent	Yield of **15a** (%)	Yield of **10a** (%)
1	5	Et_3N	MeCN	–	–
2	**20**	**Et_3N**	**MeCN**	**65**	**13**
3	20	Et_3N	DMF	–	10
4	20	KOAc	DMF	–	43
5	20	KOAc	DMF	–	–

Table 3 Summarized Results of the Heck Reactions under Optimized Conditions

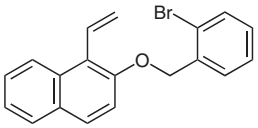
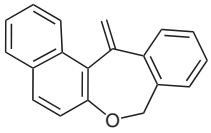
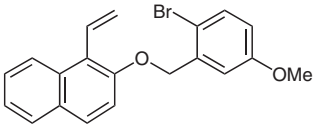
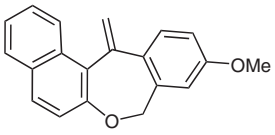
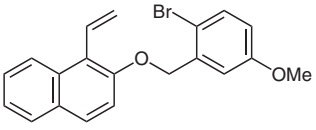
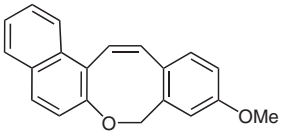
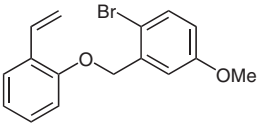
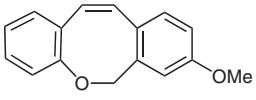
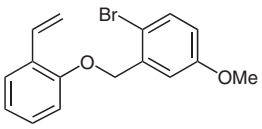
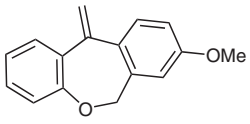
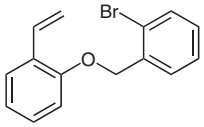
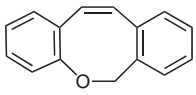
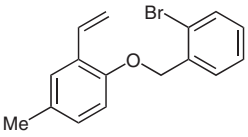
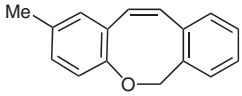
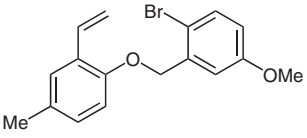
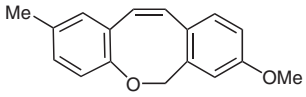
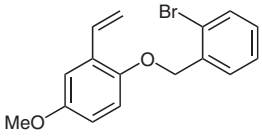
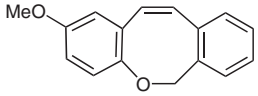
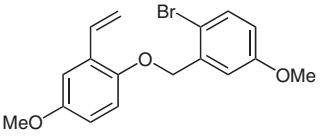
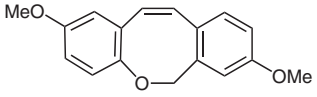
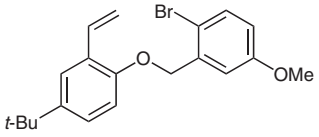
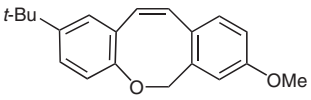
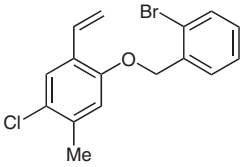
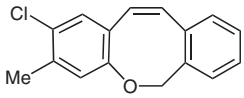
Entry	Starting material	Product (major)	Time (h)	Yield (%)	
				exo	*endo*
1	 **9a**	 **15a**	22	65	13
2	 **9b**	 **15b**	24	60	16
3[a]	 **9b**	 **10b**	3.5	trace	67
4[a]	 **9c**	 **10c**	5	trace	68
5	 **9c**	 **15c**	26	67	11

Table 3 Summarized Results of the Heck Reactions under Optimized Conditions (continued)

Entry	Starting material	Product (major)	Time (h)	Yield (%)	
				exo	*endo*
6[a]	 **9d**	 **10d**	4	–	71
7[a]	 **9e**	 **10e**	4	–	76
8[a]	 **9f**	 **10f**	5	–	70
9[a]	 **9g**	 **10g**	5	–	69
10[a]	 **9h**	 **10h**	3.5	–	66
11[a]	 **9i**	 **10i**	4	–	65
12[a]	 **9j**	 **10j**	5	–	60

[a] TBAB was used as additive.

Thus, we have demonstrated a synthetic strategy for the preparation of naphthoxepin derivatives via a Wittig olefination and intramolecular Heck reaction protocol. The product **15a** can be easily transformed into compound **7** by simple ozonolysis or sodium periodate oxidation. The antipsychotic activity of compounds **7** or **8** is well known and it has been used recently as a drug for animals. Hence its analogues may also be potentially bioactive.

In conclusion, we have developed an easy protocol for the formation of both seven-membered benzo- and naphthoxepine derivatives in an *exo-trig* mode of cyclization as well as eight-membered benzo- and naphthoxocine derivatives in very good yields via sequential Wittig olefination and phosphine-free intramolecular Heck reaction.

Melting points were determined of samples in an open capillary and are uncorrected. IR spectra of samples on KBr disks were recorded on a Perkin-Elmer L 120-000A spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300 and Bruker DPX-400 spectrometer; samples were prepared as solns in $CDCl_3$ with TMS as internal standard. CHN elemental analyses were recorded on a Perkin-Elmer 2400 series II CHN analyzer. Silica gel (60–120 mesh, Spectrochem, India) was used for chromatographic separation. Silica gel G (Spectrochem, India) was used for TLC. PE refers to the fraction boiling in the range 60–80 °C.

Aldehyde 12a; Typical Procedure for the Preparation of Compounds 12a–e by the Reimer–Tiemann Reaction

$CHCl_3$ (16 mL) was added dropwise to a soln of 2-naphthol (**11a**; 14 g, 0.1 mol) and NaOH (32 g, 0.8 mol) in H_2O (40 mL) at ca. 70 °C. The reaction mixture was allowed to stir for another 1 h at the same temperature and subsequently allowed to cool. It was then transferred to a 500-mL beaker with hot H_2O and subsequently acidified with 10 N H_2SO_4. This mixture was extracted with CH_2Cl_2 (3×75 mL), washed with H_2O (2×50 mL), and dried (Na_2SO_4). The organic layer was collected and the solvent was removed by distillation. The crude material was purified by column chromatography (silica gel, PE); this afforded product **12a**. Compounds **12b–e** were prepared similarly.

2-Bromobenzyl 2-Formylaryl Ether 14b; Typical Procedure for the Preparation of Compounds 14a–j

A mixture of 1-formyl-2-naphthol (**12a**; 1.0 g, 5.81 mmol) and 2-bromo-5-methoxybenzyl bromide (**13b**; 1.63 g, 5.81 mmol) in anhyd acetone (75 mL) was refluxed for 3–4 h in the presence of anhyd K_2CO_3 and NaI. After cooling, the reaction mixture was filtered and the solvent was removed. The residual mass was extracted with CH_2Cl_2 (3×30 mL), washed with H_2O (2×40 mL) followed by brine (40 mL), and dried (Na_2SO_4). Removal of CH_2Cl_2 gave a crude product, which was chromatographed (silica gel, EtOAc–PE, 2:98); this gave compound **14b**. The other compounds **14a**,**c–j** were prepared similarly.

Compound 14a

Yield: 91%; solid; mp 131–132 °C.

IR (KBr): 1666, 2850, 2920 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.39 (s, 2 H, OCH_2), 7.22 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.33–7.37 (m, 2 H, ArH), 7.42 (dt, *J* = 6.9, 1.0 Hz, 1 H, ArH), 7.55 (dd, *J* = 8.9, 1.2 Hz, 1 H, ArH), 7.61–7.65 (m, 2 H, ArH), 7.78 (d, *J* = 8.1 Hz, 1 H, ArH), 8.05 (d, *J* = 9.2 Hz, 1 H, ArH), 9.28 (d, *J* = 8.7 Hz, 1 H, ArH), 11.01 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 340 [M^+], 342 [$M^+ + 2$].

Anal. Calcd for $C_{18}H_{13}BrO_2$: C, 63.36; H, 3.84. Found: C, 63.41; H, 3.89.

Compound 14b

Yield: 89%; solid; mp 92–93 °C.

IR (KBr): 1671, 2850, 2920 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.77 (s, 3 H, OCH_3), 5.34 (s, 2 H, OCH_2), 6.77 (dd, *J* = 8.8, 3.0 Hz, 1 H, ArH), 7.10 (d, *J* = 2.9 Hz, 1 H, ArH), 7.31 (d, *J* = 9.0 Hz, 1 H, ArH), 7.43 (t, *J* = 7.3 Hz, 1 H, ArH), 7.49 (d, *J* = 8.8 Hz, 1 H, ArH), 7.63 (t, *J* = 7.2 Hz, 1 H, ArH), 7.78 (d, *J* = 8.1 Hz, 1 H, ArH), 8.04 (d, *J* = 9.0 Hz, 1 H, ArH), 9.27 (d, *J* = 8.7 Hz, 1 H, ArH), 11.01 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 370 [M^+], 372 [$M^+ + 2$].

Anal. Calcd for $C_{19}H_{15}BrO_3$: C, 61.47; H, 4.07. Found: C, 61.39; H, 3.97.

Compound 14c

Yield: 96%; solid; mp 79–80 °C.

IR (KBr): 1671, 2850, 2921 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 5.20 (s, 2 H, OCH_2), 6.76 (dd, *J* = 8.8, 3.0 Hz, 1 H, ArH), 7.04 (d, *J* = 8.6 Hz, 1 H, ArH), 7.08 (d, *J* = 7.6 Hz, 1 H, ArH), 7.13 (d, *J* = 2.9 Hz, 1 H, ArH), 7.47 (d, 1 H, *J* = 8.8 Hz, ArH), 7.54 (dt, *J* = 8.6, 3.0 Hz, 1 H, ArH), 7.86 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH), 10.57 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 320 [M^+], 322 [$M^+ + 2$].

Anal. Calcd for $C_{15}H_{13}BrO_3$: C, 56.10; H, 4.08. Found: C, 56.19; H, 3.99.

Compound 14d

Yield: 96%; solid; mp 75–76 °C.

IR (KBr): 1670, 2850, 2923 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.23 (s, 2 H, OCH_2), 6.91–6.94 (m, 2 H, ArH), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1 H, ArH), 7.15–7.17 (m, 3 H, ArH), 7.47 (dd, *J* = 8.6, 1.5 Hz, 1 H, ArH), 7.81 (dd, *J* = 7.4, 1.2 Hz, 1 H, ArH).

MS (EI, 70 eV): *m*/*z* = 290 [M^+], 292 [$M^+ + 2$].

Anal. Calcd for $C_{14}H_{11}BrO_2$: C, 57.76; H, 3.81. Found: C, 57.85; H, 3.92.

Compound 14e

Yield: 96%; solid; mp 41–42 °C.

IR (KBr): 1673, 2851, 2920 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 5.21 (s, 2 H, OCH_2), 6.93 (d, *J* = 8.4 Hz, 1 H, ArH), 7.21 (d, *J* = 7.4 Hz, 1 H, ArH), 7.32–7.36 (m, 2 H, ArH), 7.53 (d, *J* = 7.5 Hz, 1 H, ArH), 7.59 (d, *J* = 7.8 Hz, 1 H, ArH), 7.65 (d, *J* = 1.6 Hz, 1 H, ArH), 10.55 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 304 [M^+], 306 [$M^+ + 2$].

Anal. Calcd for $C_{15}H_{13}BrO_2$: C, 59.04; H, 4.29. Found: C, 59.31; H, 4.43.

Compound 14f

Yield: 91%; solid; mp 97–98 °C.

IR (KBr): 1685, 2850, 2921 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 5.16 (s, 2 H, OCH_2), 6.75 (dd, *J* = 8.7, 3.0 Hz, 1 H, ArH), 6.93 (d, *J* = 8.4 Hz, 1 H, ArH), 7.11 (d, *J* = 3.1 Hz, 1 H, ArH), 7.34 (dd, *J* = 8.6, 2.2 Hz, 1 H, ArH), 7.46 (d, *J* = 8.8 Hz, 1 H, ArH), 7.65 (d, *J* = 2.2 Hz, 1 H, ArH), 10.54 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 334 [M^+], 336 [$M^+ + 2$].

Anal. Calcd for $C_{16}H_{15}BrO_3$: C, 57.33; H, 4.51. Found: C, 57.58; H, 4.69.

Compound 14g

Yield: 93%; solid; mp 77–78 °C.

IR (KBr): 1685, 2850, 2920 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OCH_3), 5.22 (s, 2 H, OCH_2), 6.74 (dd, *J* = 8.9, 3.1 Hz, 1 H, ArH), 6.83 (d, *J* = 8.9 Hz, 1 H, ArH), 7.08 (d, *J* = 3.0 Hz, 1 H, ArH), 7.19 (dt, *J* = 7.7, 1.6 Hz, 1 H, ArH), 7.32 (dt, *J* = 7.7, 1.0 Hz, 1 H, ArH), 7.44 (d, *J* = 7.6 Hz, 1 H, ArH), 7.59 (dd, *J* = 8.6, 1.0 Hz, 1 H, ArH), 10.56 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 320 [M^+], 322 [$M^+ + 2$].

Anal. Calcd for $C_{15}H_{13}BrO_3$: C, 56.10; H, 4.08. Found: C, 56.31; H, 4.01.

Compound 14h

Yield: 87%; solid; mp 74–75 °C.

IR (KBr): 1678, 2850, 2921 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 5.15 (s, 2 H, OCH_2), 6.76 (dd, *J* = 8.8, 3.0 Hz, 1 H, ArH), 6.99 (d, *J* = 9.0 Hz, 1 H, ArH), 7.08 (d, *J* = 3.0 Hz, 1 H, ArH), 7.12 (dd, *J* = 8.9, 3.0 Hz, 1 H, ArH), 7.35 (d, *J* = 3.0 Hz, 1 H, ArH), 7.46 (d, *J* = 8.8 Hz, 1 H, ArH), 10.54 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 350 [M^+], 352 [$M^+ + 2$].

Anal. Calcd for $C_{16}H_{15}BrO_4$: C, 54.72; H, 4.31. Found: C, 54.81; H, 4.44.

Compound 14i
Yield: 89%; solid; mp 80–81 °C.

IR (KBr): 1680, 2850, 2923 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, $C(CH_3)_3$) 3.81 (s, 3 H, OCH_3), 5.16 (s, 2 H, OCH_2), 6.74 (dd, *J* = 8.7, 3.0 Hz, 1 H, ArH), 6.95 (d, *J* = 8.6 Hz, 1 H, ArH), 7.10 (d, *J* = 3.1 Hz, 1 H, ArH), 7.34 (dd, *J* = 8.6, 2.9 Hz, 1 H, ArH), 7.45 (d, *J* = 8.7 Hz, 1 H, ArH), 7.67 (d, *J* = 2.2 Hz, 1 H, ArH), 10.56 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 376 [M^+], 378 [M^+ + 2].

Anal. Calcd for $C_{19}H_{21}BrO_3$: C, 60.49; H, 5.61. Found: C, 60.67; H, 5.60.

Compound 14j
Yield: 90%; solid; mp 128–129 °C.

IR (KBr): 1679, 2852, 2922 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 5.21 (s, 2 H, OCH_2), 6.86 (d, *J* = 9.0 Hz, 2 H, ArH), 6.94 (s, 1 H, ArH), 7.35 (t, *J* = 6.9 Hz, 2 H, ArH), 7.81 (s, 1 H, ArH), 10.69 (s, 1 H, CHO).

MS (EI, 70 eV): *m*/*z* = 338 [M^+], 340 [M^+ + 2].

Anal. Calcd for $C_{15}H_{12}BrClO_2$: C, 53.05; H, 3.56. Found: C, 53.26; H, 3.33.

2-Bromobenzyl 2-Vinylaryl Ether 9b; Typical Procedure for the Synthesis of Compounds 9b–j by Wittig Olefination Reaction
The Wittig salt $MePPh_3I$ (1.63 g, 4.03 mmol) in anhyd THF (20 mL) was placed in a 25-mL round-bottom flask. A 1.6 M soln of *n*-BuLi in hexane (2.5 mL, 4.0 mmol) was added at 0 °C under a N_2 atmosphere. Compound **14b** (1.0 g, 2.69 mmol) in anhyd THF (5 mL) was added to the reaction mixture at 0 °C. Stirring was continued for 1 h at r.t. The THF was removed under reduced pressure and aq NH_4Cl (5 mL) was added. This mixture was extracted with CH_2Cl_2 (3 × 30 mL), washed with H_2O (2 × 20 mL), and dried (Na_2SO_4). CH_2Cl_2 was removed by distillation and the crude product was purified by column chromatography (silica gel, EtOAc–PE, 2:98); this gave **9b**. Compounds **9a**,**c**–**j** were obtained similarly. Compound **9a** has been reported previously.[13]

Compound 9b
Yield: 91%; solid; mp 72–73 °C.

IR (KBr): 2851, 2919 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.77 (s, 3 H, OCH_3), 5.22 (s, 2 H, OCH_2), 5.77 (dd, *J* = 11.2, 2.0 Hz, 1 H, $=CH_aH_b$), 5.81 (dd, *J* = 17.7, 2.0 Hz, 1 H, $=CH_aH_b$), 6.73 (dd, *J* = 8.7, 3.0 Hz, 1 H, CH_2=CH), 7.13–7.23 (m, 2 H, ArH), 7.27 (d, *J* = 9.0 Hz, 1 H, ArH), 7.36 (dt, *J* = 7.8, 1.0 Hz, 1 H, ArH), 7.44–7.48 (m, 2 H, ArH), 7.75 (d, *J* = 9.0 Hz, 1 H, ArH), 7.78 (d, *J* = 8.2 Hz, 1 H, ArH), 8.18 (d, *J* = 8.5 Hz, 1 H, ArH).

MS (EI, 70 eV): *m*/*z* = 368 [M^+], 370 [M^+ + 2].

Anal. Calcd for $C_{20}H_{17}BrO_2$: C, 65.05; H, 4.64. Found: C, 65.16; H, 4.59.

Compound 9c
Yield: 89%; solid; mp 55–56 °C.

IR (KBr): 2850, 2921 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.77 (s, 3 H, OCH_3), 5.11 (s, 2 H, OCH_2), 5.28 (dd, *J* = 11.2, 1.4 Hz, 1 H, $=CH_aH_b$), 5.75 (dd, *J* = 17.6, 1.4 Hz, 1 H, $=CH_aH_b$), 6.74 (dd, *J* = 8.7, 3.0 Hz, 1 H, CH_2=CH), 6.90 (d, *J* = 8.3 Hz, 1 H, ArH), 6.96 (t, *J* = 7.6 Hz, 1 H, ArH), 7.12–7.22 (m, 3 H, ArH), 7.45 (d, *J* = 8.8 Hz, 1 H, ArH), 7.50 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH).

MS (EI, 70 eV): *m*/*z* = 318 [M^+], 320 [M^+ + 2].

Anal. Calcd for $C_{16}H_{15}BrO_2$: C, 60.21; H, 4.74. Found: C, 60.33; H, 4.67.

Compound 9d
Yield: 88%; solid; mp 42–43 °C.

IR (KBr): 2851, 2922 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.18 (s, 2 H, OCH_2), 5.29 (dd, *J* = 11.2, 1.2 Hz, 1 H, $=CH_aH_b$), 5.74 (dd, *J* = 17.6, 1.2 Hz, 1 H, $=CH_aH_b$), 6.76 (dd, *J* = 8.8, 3.0 Hz, 1 H, CH_2=CH), 6.91–6.94 (m, 2 H, ArH), 7.16–7.21 (m, 2 H, ArH), 7.32 (dd, *J* = 7.4, 1.6 Hz, 1 H, ArH), 7.51–7.59 (m, 3 H, ArH).

MS (EI, 70 eV): *m*/*z* = 288 [M^+], 290 [M^+ + 2].

Anal. Calcd for $C_{15}H_{13}BrO$: C, 62.30; H, 4.53. Found: C, 62.17; H, 4.43.

Compound 9e
Yield: 94%; viscous liquid.

IR (neat): 2849, 2921 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 5.12 (s, 2 H, OCH_2), 5.26 (dd, *J* = 11.2, 1.4 Hz, 1 H, $=CH_aH_b$), 5.75 (dd, *J* = 17.7, 1.4 Hz, 1 H, $=CH_aH_b$), 6.80 (d, *J* = 8.3 Hz, 1 H, ArH), 7.01 (dd, *J* = 8.3, 2.0 Hz, 1 H, CH_2=CH), 7.10–7.19 (m, 2 H, ArH), 7.34 (dt, *J* = 7.5, 1.0 Hz, 2 H, ArH), 7.56 (dt, *J* = 7.8, 1.0 Hz, 2 H, ArH).

MS (EI, 70 eV): *m*/*z* = 302 [M^+], 304 [M^+ + 2].

Anal. Calcd for $C_{16}H_{15}BrO$: C, 63.38; H, 4.99. Found: C, 63.57; H, 5.13.

Compound 9f
Yield: 87%; solid; mp 57–58 °C.

IR (KBr): 2850, 2920 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 3.77 (s, 3 H, OCH_3), 5.07 (s, 2 H, OCH_2), 5.26 (dd, *J* = 11.2, 1.2 Hz, 1 H, $=CH_aH_b$), 5.74 (dd, *J* = 17.7, 1.2 Hz, 1 H, $=CH_aH_b$), 6.72 (dd, *J* = 8.7, 3.0 Hz, 1 H, CH_2=CH), 6.80 (d, *J* = 8.3 Hz, 1 H, ArH), 7.01 (dd, *J* = 8.3, 1.6 Hz, 1 H, ArH), 7.09–7.16 (m, 2 H, ArH), 7.31 (d, *J* = 1.4 Hz, 1 H, ArH), 7.44 (d, *J* = 8.7 Hz, 1 H, ArH).

MS (EI, 70 eV): *m*/*z* = 332 [M^+], 334 [M^+ + 2].

Anal. Calcd for $C_{17}H_{17}BrO_2$: C, 61.28; H, 5.14. Found: C, 61.13; H, 4.99.

Compound 9g
Yield: 90%; viscous liquid.

IR (neat): 2851, 2922 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 5.08 (s, 2 H, OCH_2), 5.28 (dd, *J* = 11.2, 1.2 Hz, 1 H, $=CH_aH_b$), 5.74 (dd, *J* = 17.6, 1.2 Hz, 1 H, $=CH_aH_b$), 6.76 (dd, *J* = 8.9, 3.0 Hz, 1 H, CH_2=CH), 6.84 (d, *J* = 8.9 Hz, 1 H, ArH), 7.06 (d, *J* = 3.0 Hz, 1 H, ArH), 7.09–7.19 (m, 2 H, ArH), 7.33 (dt, *J* = 7.7, 1.0 Hz, 1 H, ArH), 7.57 (dt, *J* = 7.7, 1.0 Hz, 2 H, ArH).

MS (EI, 70 eV): *m*/*z* = 318 [M^+], 320 [M^+ + 2].

Anal. Calcd for $C_{16}H_{15}BrO_2$: C, 60.21; H, 4.74. Found: C, 59.97; H, 4.81.

Compound 9h
Yield: 95%; viscous liquid.

IR (neat): 2850, 2919 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.77 (s, 6 H, OCH_3), 5.04 (s, 2 H, OCH_2), 5.28 (dd, *J* = 11.2, 1.0 Hz, 1 H, $=CH_aH_b$), 5.74 (dd, *J* = 17.6, 1.0 Hz, 1 H, $=CH_aH_b$), 6.71–6.77 (m, 2 H, CH_2=CH, ArH), 6.84 (d, *J* = 8.9 Hz, 1 H, ArH), 7.05 (d, *J* = 3.0 Hz, 1 H, ArH), 7.07–7.16 (m, 2 H, ArH), 7.43 (d, *J* = 8.7 Hz, 1 H, ArH).

MS (EI, 70 eV): *m*/*z* = 348 [M$^+$], 350 [M$^+$ + 2].

Anal. Calcd for $C_{17}H_{17}BrO_3$: C, 58.47; H, 4.91. Found: C, 58.53; H, 5.01.

Compound 9i
Yield: 90%; viscous liquid.

IR (neat): 2851, 2924 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (s, 9 H, $C(CH_3)_3$), 3.78 (s, 3 H, OCH_3), 5.09 (s, 2 H, OCH_2), 5.28 (d, *J* = 10.8 Hz, 1 H, $=CH_aH_b$), 5.77 (d, *J* = 17.7 Hz, 1 H, $=CH_aH_b$), 6.74 (d, *J* = 7.2 Hz, 1 H, ArH), 6.85 (d, *J* = 8.4 Hz, 1 H, ArH), 7.13 (m, 2 H, CH_2=CH and ArH overlapped), 7.24 (d, *J* = 7.5 Hz, 1 H, ArH), 7.45 (d, *J* = 8.7 Hz, 1 H, ArH), 7.52 (s, 1 H, ArH).

MS (EI, 70 eV): *m*/*z* = 374 [M$^+$], 376 [M$^+$ + 2].

Anal. Calcd for $C_{20}H_{23}BrO_2$: C, 64.01; H, 6.18. Found: C, 63.89; H, 6.20.

Compound 9j
Yield: 75%; solid, mp 48–49 °C.

IR (KBr): 2850, 2922 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (s, 3 H, CH_3), 5.10 (s, 2 H, OCH_2), 5.27 (d, *J* = 10.8 Hz, 1 H, $=CH_aH_b$), 5.71 (s, *J* = 17.7 Hz, 1 H, $=CH_aH_b$), 6.91 (m, 2 H, CH_2=CH and ArH overlapped), 7.10 (s, 1 H, ArH), 7.22–7.27 (m, 2 H, ArH), 7.33 (dt, *J* = 7.8, 1.0 Hz, 1 H, ArH), 7.54 (dt, *J* = 7.7, 1.0 Hz, 1 H, ArH).

MS (EI, 70 eV): *m*/*z* = 336 [M$^+$], 338 [M$^+$ + 2].

Anal. Calcd for $C_{16}H_{14}BrClO$: C, 56.92; H, 4.18. Found: C, 56.75; H, 3.88.

Naphthoxocine 10b; Typical Procedure for the Synthesis of Compounds 10b–j by the Heck Reaction
A mixture of **9b** (200 mg, 0.54 mmol), TBAB (210 mg, 0.65 mmol) and anhyd KOAc (145 mg, 1.48 mmol) was taken up in anhyd DMF (10 mL) under a N_2 atmosphere. $Pd(OAc)_2$ (12 mg, 10 mol%) was added and the mixture was stirred on an oil bath at 100 °C for ca. 4 h. The reaction mixture was cooled, H_2O (10 mL) was added, and the mixture was extracted with EtOAc (3 × 30 mL) and washed with H_2O (2 × 25 mL), followed by brine (30 mL). The organic layer was dried (Na_2SO_4), and the solvent was removed by distillation to furnish a viscous mass, which was purified by column chromatography (silica gel, EtOAc–PE, 1:99); this afforded product **10b**. The other substrates **9c–j** were similarly treated to give the corresponding products **10c–j**. Compound **10a** has been reported previously.[13]

Compound 10b
Yield: 67%; solid; mp 77–78 °C.

IR (KBr): 2851, 2923 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.75 (s, 3 H, OCH_3), 5.43 (s, 2 H, OCH_2), 6.94 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 7.13 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 7.33 (d, *J* = 6.9 Hz, 1 H, ArH), 7.34 (dd, *J* = 6.0, 1.9 Hz, 1 H, ArH), 7.36–7.38 (m, 2 H, ArH), 7.42–7.44 (m, 2 H, ArH), 7.49 (d, *J* = 8.5 Hz, 1 H, ArH), 7.63 (dd, *J* = 8.8, 2.8 Hz, 1 H, ArH), 7.91 (d, *J* = 8.4 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2, 74.5, 113.6, 113.8, 121.2, 121.7, 124.0, 124.2, 125.7, 126.2, 128.1, 129.1, 129.9, 130.7, 131.1, 131.2, 133.2, 136.5, 153.1, 158.4.

MS (EI, 70 eV): *m*/*z* = 288 [M$^+$].

Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.11; H, 5.72.

Compound 10c
Yield: 68%; solid; mp 69–70 °C.

IR (KBr): 2852, 2921 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 5.11 (s, 2 H, OCH_2), 6.40 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.51 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.86 (dd, *J* = 8.4, 2.6 Hz, 1 H, ArH), 6.91 (d, *J* = 2.5 Hz, 1 H, ArH), 6.95 (d, *J* = 7.5 Hz, 1 H, ArH), 6.98 (d, *J* = 7.6 Hz, 1 H, ArH), 7.07 (dt, *J* = 8.2, 1.4 Hz, 1 H, ArH), 7.21 (t, *J* = 8.2 Hz, 1 H, ArH), 7.23 (s, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4, 74.6, 114.4, 114.9, 120.9, 122.3, 126.3, 127.6, 127.9, 128.2, 131.1, 133.2, 135.2, 136.8, 158.7, 158.9.

MS (EI, 70 eV): *m*/*z* = 238 [M$^+$].

Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.89; H, 6.01.

Compound 10d
Yield: 71%; solid; mp 81–82 °C.

IR (KBr): 2851, 2921 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.09 (s, 2 H, OCH_2), 6.47 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.59 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.92–6.93 (m, 3 H, ArH), 7.18–7.23 (m, 2 H, ArH), 7.51–7.61 (m, 3 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 74.1, 120.9, 122.1, 125.7, 127.6, 128.1, 128.6, 128.8, 129.9, 130.0, 131.5, 135.3, 135.4, 138.6, 158.7.

MS (EI, 70 eV): *m*/*z* = 208 [M$^+$].

Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.34; H, 6.03.

Compound 10e
Yield: 76%; solid; mp 71–72 °C.

IR (KBr): 2852, 2922 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 5.14 (s, 2 H, OCH_2), 6.47 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.57 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.89 (dd, *J* = 6.0, 1.6 Hz, 2 H, ArH), 7.00 (s, 1 H, ArH), 7.24–7.36 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.3, 74.4, 120.7, 125.5, 127.5, 128.1, 128.6, 129.2, 129.7, 129.8, 131.3, 131.5, 135.5, 135.5, 138.5, 156.6.

MS (EI, 70 eV): *m*/*z* = 222 [M$^+$].

Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.19; H, 6.31.

Compound 10f
Yield: 70%; solid; mp 57–58 °C.

IR (KBr): 2851, 2922 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 5.08 (s, 2 H, OCH_2), 6.35 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.51 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.84–6.89 (m, 4 H, ArH), 7.00 (s, 1 H, ArH), 7.22 (d, *J* = 8.4 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4, 55.4, 74.9, 114.3, 114.8, 120.7, 126.2, 127.6, 127.9, 128.9, 131.1, 131.6, 133.3, 135.4, 137.0, 156.7, 158.9.

MS (EI, 70 eV): *m*/*z* = 252 [M$^+$].

Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.03; H, 6.55.

Compound 10g
Yield: 69%; solid; mp 74–75 °C.

IR (KBr): 2851, 2924 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 5.10 (s, 2 H, OCH_2), 6.42 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.63 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.88 (dd, *J* = 7.1, 3.1 Hz, 1 H, ArH), 7.05 (s, 1 H, ArH), 7.32 (dd, *J* = 6.9, 1.7 Hz, 1 H, ArH), 7.34–7.39 (m, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.7, 75.4, 114.4, 119.0, 121.7, 127.4, 127.6, 128.6, 129.0, 129.2, 129.6, 132.0, 135.9, 138.2, 153.1, 154.6.

MS (EI, 70 eV): *m*/*z* = 238 [M^+].

Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.58; H, 6.07.

Compound 10h
Yield: 66%; solid; mp 67–68 °C.

IR (KBr): 2849, 2919 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 5.04 (s, 2 H, OCH_2), 6.33 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.55 (d, *J* = 13.8 Hz, 1 H, $=CH_aH_b$), 6.66 (dd, *J* = 8.7, 3.1 Hz, 1 H, ArH), 6.73 (d, *J* = 3.1 Hz, 1 H, ArH), 6.85 (dd, *J* = 7.9, 2.8 Hz, 2 H, ArH), 6.94 (d, *J* = 8.7 Hz, 1 H, ArH), 7.22 (s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2, 55.7, 74.5, 114.3, 114.7, 119.5, 125.7, 126.2, 128.1, 128.2, 131.1, 131.2, 131.5, 133.2, 136.5, 154.0, 158.4.

MS (EI, 70 eV): *m*/*z* = 268 [M^+].

Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.19; H, 5.91.

Compound 10i
Yield: 65%; solid; mp 69–70 °C.

IR (KBr): 2850, 2921 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 9 H, $C(CH_3)_3$), 3.83 (s, 3 H, OCH_3), 5.12 (s, 2 H, OCH_2), 6.46 (d, *J* = 13.8 Hz, 2 H, CH =CH), 6.86–6.94 (m, 3 H, ArH), 7.11 (d, *J* = 8.1 Hz, 1 H, ArH), 7.18–7.25 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 34.0, 55.4, 74.4, 114.3, 114.9, 120.3, 125.3, 125.4, 127.5, 128.3, 131.2, 131.9, 133.1, 137.0, 144.8, 156.4, 158.8.

MS (EI, 70 eV): *m*/*z* = 294 [M^+].

Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.73; H, 7.51.

Compound 10j
Yield: 60%; solid; mp 88–89 °C.

IR (KBr): 2852, 2922 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3 H, CH_3), 5.16 (s, 2 H, OCH_2), 6.40 (d, *J* = 13.5 Hz, 1 H, $CH_a=CH_b$), 6.56 (d, *J* = 13.5 Hz, 1 H, $CH_a=CH_b$), 6.84 (s, 1 H, ArH), 7.15 (s, 1 H, ArH), 7.26–7.38 (m, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.5, 73.8, 123.0, 124.6, 126.9, 127.8, 128.5, 128.6, 128.9, 130.0, 131.3, 134.5, 135.0, 136.3, 138.4, 156.6.

MS (EI, 70 eV): *m*/*z* = 256 [M^+].

Anal. Calcd For $C_{16}H_{13}ClO$: C, 74.85; H, 5.10. Found: C, 74.55; H, 4.98.

Naphthoxepines 15a–c by Heck Reaction; General Procedure
A mixture of **9a** (200 mg, 0.59 mmol) and anhyd Et_3N (2 mL) was taken up in anhyd MeCN (10 mL) under a N_2 atmosphere. $Pd(PPh_3)_4$ (136 mg, 20 mol%) was added and the mixture was stirred on an oil bath under reflux for ca. 24 h. The progress of the reaction was monitored by TLC. The reaction mixture was cooled, H_2O (10 mL) was added, and the mixture was extracted with EtOAc (3 × 30 mL) and washed with H_2O (2 × 30 mL), followed by brine (30 mL). The organic layer was dried (Na_2SO_4). The solvent was removed by distillation to furnish a viscous mass, which was purified by column chromatography (silica gel, EtOAc–PE, 1:99); this afforded the product **15a**. The other substrates **9b**,**c** were similarly treated to give products **15b**,**c**.

Compound 15a
Yield: 65%; gummy.

IR (neat): 2873, 2927 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.36 (s, 2 H, OCH_2), 5.61 (s, 1 H, $=CH_aH_b$), 5.90 (s, 1 H, $=CH_aH_b$), 7.00–7.15 (m, 2 H, ArH), 7.30–7.36 (m, 3 H, ArH), 7.45 (t, *J* = 7.16 Hz, 1 H, ArH), 7.53 (d, *J* = 7.24 Hz, 1 H, ArH), 7.68 (d, *J* = 8.8 Hz, 1 H, ArH), 7.75 (d, *J* = 7.96 Hz, 1 H, ArH), 8.34 (d, *J* = 8.56 Hz, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 71.7, 114.9, 120.8, 120.9, 123.6, 123.9, 124.0, 124.9, 125.0, 126.2, 126.4, 127.2, 127.8, 128.2, 128.5, 129.4, 131.7, 137.2, 153.3.

MS (EI, 70 eV): *m*/*z* = 281 [M^+ + Na].

Anal. Calcd for $C_{19}H_{14}O$: C, 88.34; H, 5.46. Found: C, 88.28; H, 5.72.

Compound 15b
Yield: 60%; gummy.

IR (neat): 2853, 2926 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 5.44 (s, 2 H, OCH_2), 6.75 (d, *J* = 2.4 Hz, 1 H, $=CH_aH_b$), 6.78 (d, *J* = 2.7 Hz, 1 H, $=CH_aH_b$), 6.95 (m, 2 H, ArH), 7.14 (d, *J* = 8.4 Hz, 1 H, ArH), 7.20 (d, *J* = 9.0 Hz, 1 H, ArH), 7.34 (t, *J* = 7.2 Hz, 1 H, ArH), 7.45 (t, *J* = 7.8 Hz, 1 H, ArH), 7.63 (d, *J* = 9.0 Hz, 1 H, ArH), 7.72 (d, *J* = 8.1 Hz, 1 H, ArH), 7.92 (d, *J* = 8.4 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 54.1, 70.0, 111.5, 112.3, 113.9, 118.3, 119.8, 121.0, 122.6, 123.3, 125.4, 127.2, 127.7, 128.4, 128.5, 129.3, 131.4, 137.9, 152.3, 158.7.

MS (EI, 70 eV): *m*/*z* = 288 [M^+].

Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.02; H, 5.61.

Compound 15c
Yield: 67%; gummy.

IR (neat): 2852, 2922 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 5.12 (s, 2 H, OCH_2), 5.21 (s, 1 H, $=CH_aH_b$), 5.64 (s, 1 H, $=CH_aH_b$), 6.81–6.86 (m, 3 H, ArH), 6.90 (t, *J* = 7.2 Hz, 1 H, ArH), 7.13–7.17 (m, 1 H, ArH), 7.28 (d, *J* = 8.04 Hz, 1 H, ArH), 7.42 (dd, *J* = 7.8, 1.16 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3, 70.2, 112.5, 112.8, 113.4, 114.5, 119.5, 121.0, 126.6, 127.2, 128.9, 129.6, 133.2, 138.8, 155.9, 159.8.

MS (EI, 70 eV): *m*/*z* = 238 [M^+].

Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.94; H, 6.07.

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