HETEROCYCLES, Vol. 86, No. 2, 2012, pp. 1555 - 1563. © 2012 The Japan Institute of Heterocyclic Chemistry
Received, 4th July, 2012, Accepted, 21st August, 2012, Published online, 4th September, 2012
DOI: 10.3987/COM-12-S(N)89

# DIVERSITY ORIENTED APPROACH TO 9-ARYL-SUBSTITUTED NAPHTHOXEPINE DERIVATIVES VIA CLAISEN REARRANGEMENT, RING-CLOSING METATHESIS AND SUZUKI–MIYAURA CROSS-COUPLING AS KEY STEPS†

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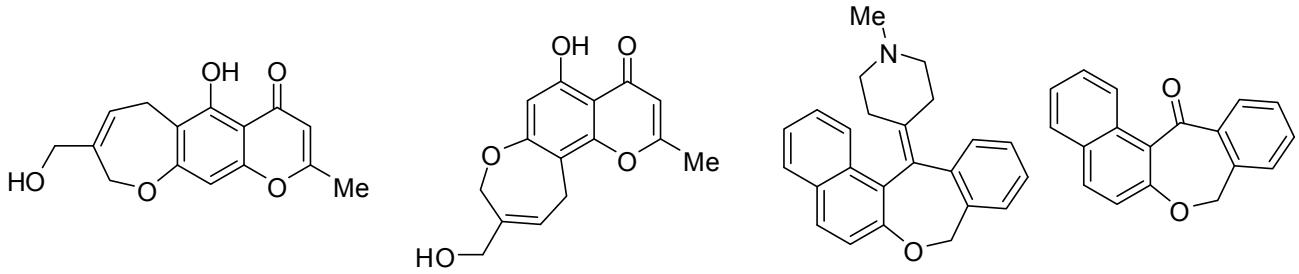
**Abstract** – A novel route to a variety of 9-aryl-substituted naphthoxepine derivatives is described starting with 6-bromo-2-naphthol *via* Claisen rearrangement (CR), ring-closing metathesis (RCM) and Suzuki−Miyaura (SM) cross-coupling as key steps.

Oxepines are core structural units present in several of biologically active natural products such as brevetoxin, gambierol, and ciguatoxin, which show potent antiviral and antifungal activities.[1-4] A few natural products **1-4** containing oxepine unit are depicted in Figure 1.[2] For example, the construction of (-)-clavizepine has been achieved *via* a benzoxepine intermediate.[3]




ptaeroxylinol (**1**) eranthin (**2**) **3** **4**

**Figure 1.** Natural products **1-4** comprising oxepine skeleton

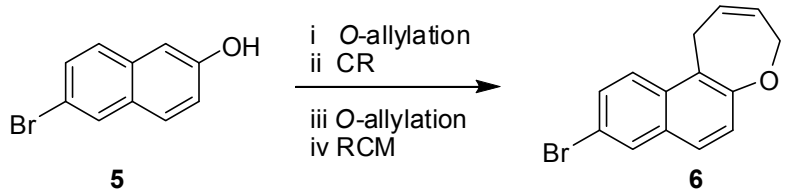
Since the oxepine derivatives are useful building blocks, several efforts are directed towards their synthesis and these methods[4] include: (i) base-catalyzed cyclization of allenyl sulfoxides/sulfones, (ii)

†This paper is dedicated to Prof. Dr. Ei-ichi Negishi on the occasion of his 77th birthday

carbocyclization by rhodium-catalysis, (iii) intramolecular acyl radical cyclization, (iv) Lewis-acid catalyzed intramolecular cyclization. However, these routes require the usage of expensive catalyst and require high temperature affording the products in low yields.

In view of some of the limitations towards the synthesis of naphthoxepine derivatives and also our interest in these molecules, we have conceived a strategy based on Claisen rearrangement (CR), ring-closing metathesis (RCM) and Suzuki–Miyaura cross-coupling (SM) as key steps. Since CR, olefin metathesis and SM coupling are considered catalytic processes, utilization of these strategies in a synthetic sequence increases the 'green content' of the overall synthesis.

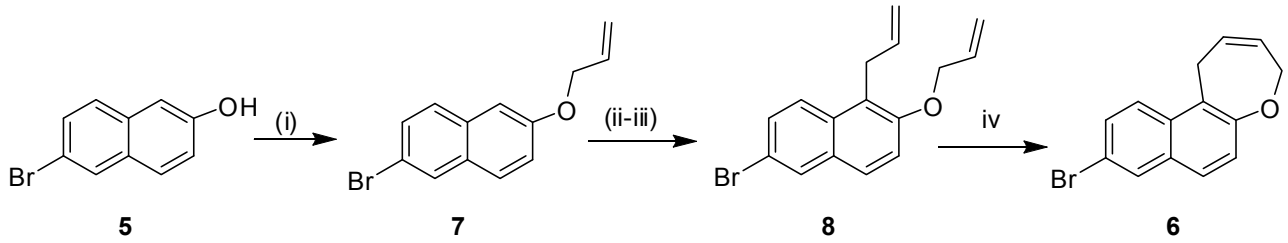
During the past two decades, olefin metathesis has drawn considerable attention because of a wide range of transformations that are possible with commercially available and easy to handle catalysts. A variety of retrosynthetic paths are opened to carbocycles, polycyclics and macrocycles by incorporating the RCM reaction sequence.[5-6] Based on the above considerations, we have designed a novel approach to oxepine derivative **6** by employing the inexpensive *β*-naphthol derivative **5** as starting material. In this regard *O*-allylation, microwave (MW) assisted CR and finally the RCM as key steps (Scheme 1) can generate the known building block **6**.[7] The SM cross-coupling can be performed at different stages of the synthetic sequence.




**5** **6**

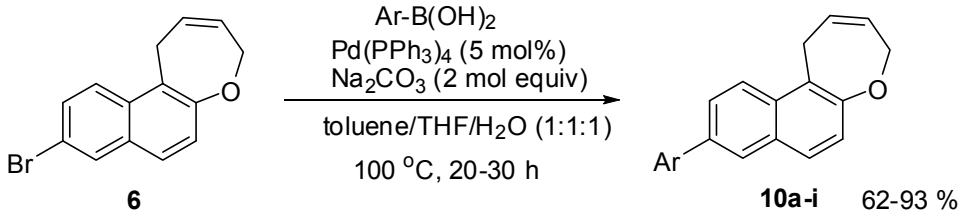
**Scheme 1.** Synthesis of naphthoxepine **6**

Our strategy to oxepine derivative **6** starts with 6-bromo-2-naphthol (**5**) as the starting precursor. To this end, 6-bromo-2-naphthol (**5**) was *O*-allylated by using allyl bromide/$K_2CO_3$ in acetone to yield the desired product **7** (98%). Later, the MW-assisted CR of allyl derivative **7** followed by *O*-allylation gave the diallyl derivative **8** (93%).[7b] Since Grubbs catalyst **9** is expensive, our initial intention was to perform the metathesis step at the end of the synthetic sequence. In this regard, diallyl compound **8** was treated with phenylboronic acid under Pd(0) conditions. Unfortunately, a mixture of compounds was formed. So, it was decided to prepare the RCM product first and then attempt the SM coupling[8] as a last step. To prepare the 9-bromo-naphthoxepine (**6**) required for the SM coupling reaction, the diallylated compound **8** was subjected to RCM in the presence of Grubbs first generation catalyst (**9**, 5 mol%) in dichloromethane (Scheme 2) to generate the compound **6** in 96% yield.[7b]




**Scheme 2.** Synthetic approach towards the RCM product **6**. *Reaction conditions:* (i) allyl bromide, $K_2CO_3$, acetone, rt, 14 h, 98%; (ii) silica gel supported MWI (800W) assisted CR, 8 min, 88%; (iii) allyl bromide, $K_2CO_3$, acetone, rt, 16 h, 93%; (iv) $(Cy_3P)_2Cl_2Ru$ = CHPh [**9**, 5.0 mol%], DCM, rt, 4 h, 96%.

The bromo compound **6** was treated with phenylboronic acid in the presence of $Pd(PPh_3)_4$ (5.0 mol%), $Na_2CO_3$ (2.0 equiv) in toluene/THF/water (1:1:1) as the solvent mixture to furnish the cross-coupling product **10a** in an excellent yield (90%, Scheme 3).[8b] Later, the substrate scope has been expanded by employing various arylboronic acids under similar conditions to generate the desired 9-arylnaphthoxepine derivatives **10b-i** in moderate to excellent yield.




**Scheme 3.** Synthesis of diverse SM coupling products **10a-i**

All these final products were characterized by $^1$H NMR/$^{13}$C NMR spectral data. Among these products obtained, phenyl- and 3-methylphenyl-substituted derivatives **10a-b** were formed in excellent yield (86-90%) while the 4-formylphenyl (electron withdrawing) and 4-bromophenyl-based derivatives **10c-d** were accomplished in slightly lower yield (75-80%) compared to **10a-b** (Figure 2). In addition, 3-thiophene-based SM cross-coupling product **10e** was also obtained in a moderate yield (62%). However, heteroaromatic cross-coupling compounds **10h-i** were obtained in excellent yields. Due to the presence of different functional groups, these coupling products can be used for further synthetic manipulation to generate biologically useful molecules.

In conclusion, we have disclosed a simple and mild synthetic strategy to novel 9-arylnaphthoxepine adducts *via* CR, RCM and SM reaction as key steps. These products are obtained in very good yields. The scope of this reaction can be further extended because some of these SM-cross coupling products contain additional functionalities for further synthetic manipulation.

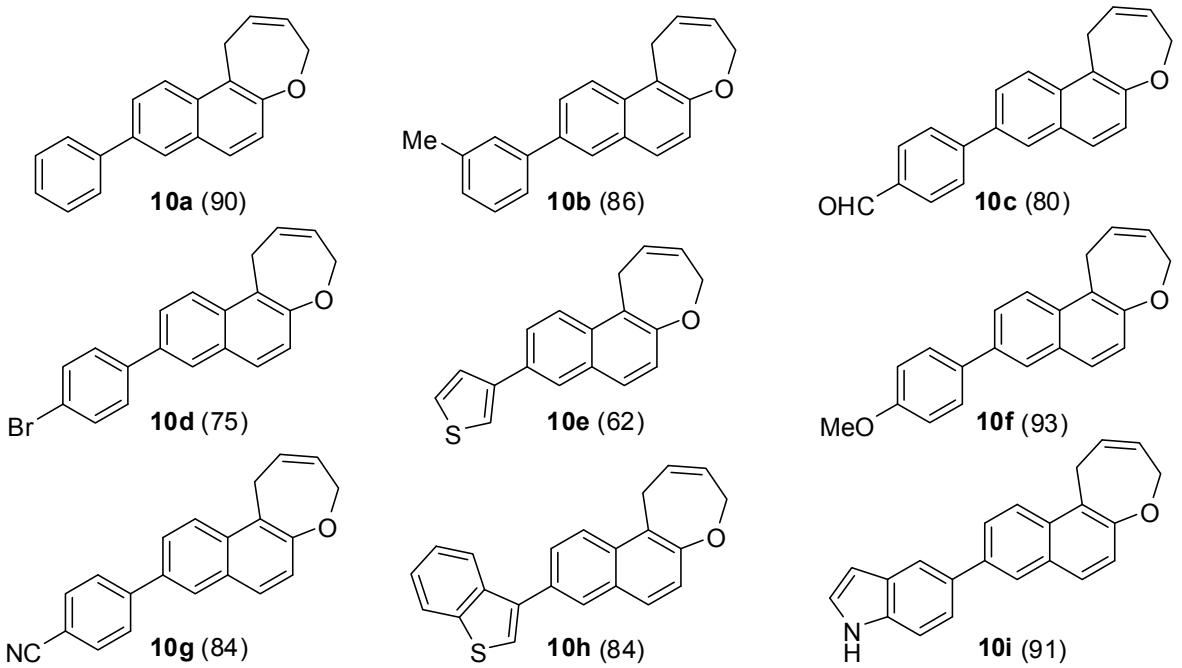



**Figure 2.** List of SM cross-coupling products (**10a-i**) obtained from **6**. Yields are given in the parentheses.

## EXPERIMENTAL

Melting points were recorded on Labhosp or Veego melting point apparatus. Infrared (IR) spectra were recorded on Nicolet Impact-400 FT IR spectrometer in KBr/$CHCl_3$/$CCl_4$. $^1$H NMR (400 MHz), $^{13}$C NMR (100 MHz or 75 MHz) spectral data were determined at r.t. on AV 400 (Bruker) or Varian in $CDCl_3$ solution. Coupling constants (*J* values) are given in Hertz (Hz). The high-resolution mass measurements were carried out using Micromass Q-Tof spectrometer. Analytical thin layer chromatography (TLC) was performed on (10 × 5 cm) glass plates coated with Acme's silica gel G or GF 254 (containing 13% calcium sulfate as a binder). Column chromatography was performed using Acme's silica gel (100-200 mesh) using double spray bellows for application of pressure and the column is eluted with ethyl acetate-petroleum ether mixture. Solvents used in this study were dried over appropriate drying agents and distilled prior to use. Compound **6** was prepared according to the reported procedure.[7b]

### Suzuki−Miyaura cross-coupling reaction: General procedure

To a solution of bromo derivative **6** (1.0 equiv.) in THF/toluene/water (1:1:1) was added $Na_2CO_3$ (3-4 equiv.) and arylboronic acid (2.0 equiv.). The reaction mixture was degassed with nitrogen for 20 minutes. The catalyst $Pd(PPh_3)_4$ (5 mol%) was subsequently added and the reaction mixture was heated at 100 °C (oil bath temperature). After completion of the reaction (12-30 h, TLC monitoring), the solvent was removed under reduced pressure and the residue was diluted with EtOAc. The organic layer was washed with water (10 mL), brine (10 mL) and dried over $Na_2SO_4$. The solvent was evaporated and the crude

product was purified by silica gel column chromatography (EtOAc/petroleum ether).

**9-Phenyl-1,4-dihydronaphtho[2,1-*b*]oxepine (10a)**: This compound was prepared according to the general procedure by treating the compound **6** (50 mg, 0.18 mmol) in THF-toluene (1:1) mixture (12 mL), aq. $Na_2CO_3$ (77 mg, 0.73 mmol), with phenylboronic acid (44 mg, 0.36 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) (heating at 100 °C for 20 h). The crude product was purified by silica gel column chromatography (2% EtOAc-petroleum ether) to give the desired coupling product **10a** (44.2 mg, 90%) as a colorless solid; $R_f$ = 0.45 (silica gel, 5% EtOAc-petroleum ether); Mp 143-144 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.26-3.32 (m, 1H), 3.67-3.73 (m, 1H), 5.27 (d, $J$ = 10.3 Hz, 1H), 5.39-5.48 (m, 2H), 6.08-6.16 (m, 1H), 7.15 (d, $J$ = 8.8 Hz, 1H), 7.34-7.39 (m, 1H), 7.45-7.53 (m, 2H), 7.63-7.79 (m, 5H), 8.01 (d, $J$ = 1.3 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 34.9, 84.5, 112.7, 117.1, 118.2, 123.4, 124.3, 126.6, 126.9, 127.2, 127.4, 127.5, 129.0, 129.6, 129.7, 130.1, 135.8, 137.6, 141.4, 157.3; IR (KBr): $\tilde{\nu}$ = 3020, 1602, 1519, 1473, 1421, 1216, 1017 cm$^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{20}H_{17}O$ $[M+H]^+$ 273.1279; found: 273.1277.

**9-*m*-Tolyl-1,4-dihydronaphtho[2,1-*b*]oxepine (10b)**: This compound was prepared according to the general procedure by treating the compound **6** (50 mg, 0.18 mmol) in THF-toluene (1:1) mixture (10 mL), aq. $Na_2CO_3$ (77 mg, 0.73 mmol), with 3-methylphenylboronic acid (49 mg, 0.36 mmol) and $Pd(PPh_3)_4$ (11 mg, 0.01 mmol) (heating at 100 °C for 18 h). Purification of the crude material by silica gel column chromatography (1% EtOAc-petroleum ether) gave the desired coupling product **10b** (45 mg, 86%) as a gummy solid; $R_f$ = 0.28 (silica gel, petroleum ether); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 2.46 (s, 3H), 3.27-3.33 (m, 1H), 3.67-3.73 (m, 1H), 5.28 (d, $J$ = 10.4 Hz, 1H), 5.39-5.49 (m, 2H), 6.09-6.18 (m, 1H), 7.17 (t, $J$ = 8.8 Hz, 2H), 7.36-7.39 (m, 1H), 7.49-7.54 (m, 2H), 7.63 (d, $J$ = 8.6 Hz, 1H), 7.73-7.79 (m, 2H), 8.02 (d, $J$ = 1.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 21.8, 34.9, 84.5, 112.6, 117.1, 118.2, 123.3, 124.5, 126.6, 126.8, 127.9, 128.1, 128.9, 129.6, 129.7, 130.1, 135.9, 137.6, 138.6, 141.4, 157.2; IR (neat): $\tilde{\nu}$ = 3053, 2986, 2926, 2854, 1631, 1603, 1491, 1421, 1265, 1096 cm$^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{21}H_{19}O$ $[M+H]^+$ 287.1436; found: 287.1446.

**4-(1,4-Dihydronaphtho[2,1-*b*]oxepin-9-yl)benzaldehyde (10c)**: This compound was prepared according to the general procedure by treating the compound **6** (30 mg, 0.11 mmol) in THF-toluene-water (1:1:1), $Na_2CO_3$ (46 mg, 0.44 mmol) with 4-formylphenylboronic acid (32.7 mg, 0.22 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) heating at 100 °C for 18 h. Purification of the crude material by silica gel column chromatography (1.5% EtOAc-petroleum ether) gave the desired coupling product **10c** (26 mg, 80%) as a colorless solid; $R_f$ = 0.45 (silica gel, 10% EtOAc-petroleum ether); Mp 122-124 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.31-3.33 (m, 1H), 3.72-3.74 (m, 1H), 5.28 (d, $J$ = 10.2 Hz, 1H), 5.31-5.48 (m, 2H), 6.08-6.17 (m, 1H), 7.19 (d, $J$ = 8.8 Hz, 1H), 7.68 (d, $J$ = 8.8, 1H), 7.78 (dt, $J_1$ = 8.4, $J_2$ = 2.0 Hz, 2H), 7.87 (d, $J$ = 8.4 Hz, 2H), 7.99 (d, $J$ = 8.0 Hz, 2H), 8.09 (s, 1H), 10.10 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$

= 34.8, 84.6, 113.1, 117.2, 118.4, 123.8, 126.1, 127.7, 127.8, 129.5, 129.9, 130.6, 130.7, 134.1, 135.1, 137.5, 147.4, 157.9, 192.1; IR (KBr): $\tilde{\nu}$ = 3020, 1698, 1602, 1522, 1424, 1216 $cm^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{21}H_{17}O_2$ $[M+H]^+$ 301.1229; found: 301.1219.

**9-(4-Bromophenyl)-(1,4-dihydronaphtho[2,1-*b*]oxepine (10d)**: This compound was prepared according to the general procedure by treating the compound **6** (100 mg, 0.36 mmol) in THF-toluene-water (1:1:1) mixture (20 mL), $Na_2CO_3$ (154 mg, 1.5 mmol) with 4-bromophenylboronic acid (110 mg, 0.55 mmol) and $Pd(PPh_3)_4$ (21 mg, 0.02 mmol) heating at 100 °C for 24 h. Purification of the crude material by silica gel column chromatography (0.2% EtOAc-petroleum ether) gave the desired coupling product **10d** (95 mg, 75%) as a colorless solid; $R_f$ = 0.22 (silica gel, petroleum ether); Mp 118-120 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.26-3.32 (m, 1H), 3.67-3.73 (m, 1H), 5.28 (d, *J* = 10.4 Hz, 1H), 5.39-5.48 (m, 2H), 6.07-6.16 (m, 1H), 7.16 (d, *J* = 8.8 Hz, 1H), 7.47-7.75 (m, 7H), 7.98 (d, *J* = 1.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 34.8, 84.4, 112.8, 117.0, 118.2, 121.3, 123.5, 126.0, 126.7, 128.8, 129.6, 130.2, 132.0, 134.5, 137.5, 140.2, 157.4; IR (KBr): $\tilde{\nu}$ = 3055, 2978, 2296, 1626, 1497, 1265, 1074 $cm^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{20}H_{16}OBr$ $[M+H]^+$ 351.0385; found: 351.0380.

**9-(Thiophen-3-yl)-1,4-dihydronaphtho[2,1-*b*]oxepine (10e)**: This compound was prepared according to the general procedure by treating the compound **6** (50 mg, 0.18 mmol) in THF-toluene-water (1:1:1) mixture (10 mL), $Na_2CO_3$ (77 mg, 0.73 mmol) with 3-thienylboronic acid (46.5 mg, 0.36 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) heating at 100 °C for 22 h. Purification of the crude material by silica gel column chromatography (1.5% EtOAc-petroleum ether) gave the desired coupling product **10e** (31 mg, 62%) as a white solid; $R_f$ = 0.49 (silica gel, 5% EtOAc-petroleum ether); Mp 138-140 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.26-3.32 (m, 1H), 3.66-3.72 (m, 1H), 5.30 (d, *J* = 10.4 Hz, 1H), 5.31-5.49 (m, 2H), 6.10-6.18 (m, 1H), 7.16 (d, *J* = 8.7 Hz, 1H), 7.43-7.7.45 (m, 1H), 7.51-7.54 (m, 2H), 7.6 (d, *J* = 8.6 Hz, 1H), 7.74 (d, *J* = 1.8 Hz, 1H), 7.76 (d, *J* = 1.8 Hz, 1H), 8.02 (d, *J* = 1.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 34.7, 84.3, 112.5, 116.9, 118.2, 119.9, 123.3, 125.7, 125.9, 126.3, 126.4, 129.3, 129.5, 129.9, 130.4, 137.4, 142.4, 157.1; IR (KBr): $\tilde{\nu}$ = 3054, 2986, 2685, 1604, 1421, 1266, 1155 $cm^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{18}H_{15}OS$ $[M+H]^+$ 279.0844; found: 279.0856.

**9-(4-Methoxyphenyl-1,4-dihydronaphtho[2,1-*b*]oxepine (10f)**: This product was obtained according to the general procedure by treating the compound **6** (65 mg, 0.24 mmol) in THF-toluene-water (1:1:1) mixture (12 mL), $Na_2CO_3$ (100 mg, 0.95 mmol) with 4-methoxyphenylboronic acid (72 mg, 0.5 mmol) and $Pd(PPh_3)_4$ (14 mg, 0.01 mmol) heating at 100 °C for 26 h. Purification of the crude material by silica gel column chromatography (2% EtOAc-petroleum ether) gave the desired coupling product **10f** (67 mg, 93%) as a colorless solid; $R_f$ = 0.45 (silica gel, 5% EtOAc-petroleum ether); Mp 150-152 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.28 (dd, *J* = 15.3 Hz, *J* = 7.6 Hz, 1H), 3.69 (dd, *J* = 15.3 Hz, *J* = 10.4 Hz, 1H),

3.85 (s, 3H), 5.27 (d, $J$ = 10.4 Hz, 1H), 5.38-5.47 (m, 2H); 6.08-6.16 (m, 1H), 6.96 (d, $J$ = 8.4 Hz, 1H), 7.02 (d, $J$ = 9.2 Hz, 1H), 7.14 (d, $J$ = 8.8 Hz, 1H), 7.48 (d, $J$ = 8.8 Hz, 1H), 7.62-7.64 (m, 2H), 7.69-7.73 (m, 2H), 7.96 (d, $J$ = 1.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 34.9, 55.5, 84.4, 112.6, 114.3, 114.5, 117.0, 118.2, 123.4, 126.1, 126.5, 127.9, 128.4, 129.4, 129.8, 133.7, 133.9, 135.5, 137.7, 157.1, 158.9; IR (KBr): $\tilde{\nu}$ = 3054, 2986, 2685, 2305, 1607, 1551, 1421, 1264, 1156 cm$^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{21}H_{19}O_2$ $[M+H]^+$ 303.1385; found: 303.1390.

**4-(1,4-Dihydronaphtho[2,1-*b*]oxepin-9-yl)benzonitrile (10g)**: This compound was prepared according to the general procedure by treating the compound **6** (35 mg, 0.13 mmol), $Na_2CO_3$ (55 mg, 0.51 mmol) with 4-cyanophenylboronic acid (37.4 mg, 0.25 mmol), in THF-toluene-water (1:1:1) mixture (12 mL) and $Pd(PPh_3)_4$ (14.7 mg, 0.013 mmol). The reaction mixture was heated at 100 °C for 24 h. The crude product was purified by silica gel column chromatography (2.5% EtOAc-petroleum ether) to give the desired coupling product **10g** (31 mg, 84%) as a colorless solid; $R_f$ = 0.22 (silica gel, 5% EtOAc-petroleum ether); Mp 147-150 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.27-3.33 (m, 1H), 3.68-3.75 (m, 1H), 5.29 (d, $J$ = 10.4 Hz, 1H), 5.44-5.49 (m, 2H), 6.08-6.17 (m, 1H), 7.19 (d, $J$ = 8.8 Hz, 1H), 7.66-7.80 (m, 7H), 8.03 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 34.8, 84.6, 110.7, 113.2, 117.2, 118.4, 119.2, 123.9, 125.8, 127.6, 127.8, 129.5, 129.9, 130.8, 132.8, 133.6, 137.4, 145.9, 158.0; IR (KBr): $\tilde{\nu}$ = 3054, 2986, 2923, 2227, 1603, 1503, 1421, 1265 cm$^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{21}H_{16}NO$ $[M+H]^+$ 298.1232; found: 298.1225.

**9-(Benzo[*b*]thiophen-3-yl)-1,4-dihydronaphtho[2,1-*b*]oxepine (10h)**: This compound was prepared according to the general procedure by treating the compound **6** (50 mg, 0.18 mmol), $Na_2CO_3$ (77 mg, 0.73 mmol) with benzothiophene-3-boronic acid (65 mg, 0.36 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) in THF-toluene-water (1:1:1) mixture (10 mL). It was heated at 100 °C for 25 h. Purification of the crude material by silica gel column chromatography (1% EtOAc-petroleum ether) gave the desired coupling product **10h** (50 mg, 84%) as a colorless solid; $R_f$ = 0.1 (silica gel, petroleum ether); Mp 153-158 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.27 (dd, $J$ = 15.3 Hz, $J$ = 7.6 Hz, 1H), 3.68 (d, $J$ = 15.3 Hz, $J$ = 9.6 Hz, 1H), 5.28 (dt, $J_1$ = 10.2 Hz, $J_2$ = 1.2 Hz, 1H), 5.39-5.47 (m, 2H), 6.07-6.16 (m, 1H), 7.15 (d, $J$ = 8.7 Hz, 1H), 7.28-7.32 (m, 2H), 7.58-7.78 (m, 4H), 7.82-7.85 (m, 2H), 8.11 (d, $J$ = 1.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 34.9, 84.6, 113.0, 117.2, 118.6, 119.3, 122.4, 123.5, 123.6, 124.4, 124.7, 125.4, 126.5, 129.0, 129.5, 129.7, 130.7, 137.5, 139.5, 141.0, 144.7, 157.7; IR (KBr): $\tilde{\nu}$ = 3054, 2986, 1421, 1265 cm$^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{22}H_{17}OS$ $[M+H]^+$ 329.1000; found: 329.1004.

**5-(1,4-Dihydronaphtho[2,1-*b*]oxepin-9-yl)-1*H*-indole (10i)**: This compound was prepared according to the general procedure by treating the compound **6** (35 mg, 0.13 mmol) with indole-5-boronic acid (41 mg, 0.25 mmol), $Na_2CO_3$ (54 mg, 0.5 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) in THF-toluene-water (1:1:1)

mixture (8 mL). The reaction mixture was heated at 100 °C for 30 h. Purification of the crude material by silica gel column chromatography (2% EtOAc-petroleum ether) gave the desired coupling product **10i** (36.2 mg, 91%) as a colorless solid; $R_f$ = 0.38 (silica gel, 5% EtOAc-petroleum ether); Mp 160-163 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.26-3.34 (m, 1H), 3.67-3.73 (m, 1H), 5.27 (dt, $J_1$ = 10.4 Hz, $J_2$ = 1.1 Hz, 1H), 5.38-5.47 (m, 2H), 6.08-6.17 (m, 1H), 6.62-6.64 (m, 1H), 7.14 (d, $J$ = 8.8 Hz, 1H), 7.23-7.25 (m, 1H), 7.45-7.48 (m, 1H), 7.55-7.57 (m, 1H), 7.64 (dd, $J_1$= $J_2$ = 8.5 Hz, 1H), 7.74 (d, $J$ = 8.6 Hz, 1H), 7.82 (dd, $J_1$= 8.6 Hz, $J_2$ = 1.9 Hz, 1H), 7.95-7.96 (m, 1H), 8.05 (d, $J$ = 1.8 Hz, 1H), 8.19 (br, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 34.9, 84.4, 103.2, 111.5, 112.5, 117.0, 118.1, 119.4, 122.2, 123.2, 125.0, 126.6, 127.3, 128.7, 129.4, 129.7, 129.9, 133.6, 135.4, 137.2, 137.7, 156.9; IR (KBr): $\tilde{\nu}$ = 3475, 3053, 2986, 2253, 1605, 1481, 1422, 1263, 1093 cm$^{-1}$; HRMS (Q-Tof): *m/z* calcd for $C_{22}H_{18}NO$ $[M+H]^+$ 312.1388; found: 312.1401.

## ACKNOWLEDGEMENTS

We thank Department of Science and Technology (DST), New Delhi, and Industrial Research and Consultancy Centre (IRCC), IIT-Bombay for financial support. We also thank Sophisticated Analytical Instrument Facility (SAIF), IIT-Bombay for recording spectral data. S. K. thanks Department of Science and Technology for the award of a J. C. Bose fellowship. N. G. K. thanks Department of Chemistry, IIT-Bombay for awarding the research fellowship.

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