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## Diversity-oriented approach to natural product inspired pyrano-carbazole derivatives: Strategic utilization of hetero-Diels–Alder reaction, Fischer indolization and the Suzuki–Miyaura cross-coupling reaction

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**ABSTRACT:** A variety of natural products inspired pyrano-carbazole derivatives have been assembled *via* hetero-Diels–Alder reaction and Fischer indolization (FI) under operationally simple reaction conditions. Later, the scope of this methodology has been expanded through Suzuki–Miyaura cross-coupling reaction involving different boronic acids. This simple strategy can be useful to generate a variety of medicinally important carbazole derivatives.

## Graphical abstract



#### **1. Introduction**

Generating a library of architecturally complex frameworks with minimum number of steps in a diversity-oriented fashion<sup>1</sup> is an important tactic for assembling "drug-like" small molecules.<sup>2</sup> The pioneering work in this area has been done by Schreiber and co-workers to establish a diverse collection of nitrogen-containing small molecules with the applications in drug discovery and chemical genetics.<sup>3</sup> Among the heterocycles, nitrogen containing compounds are considered as privileged core structural units present in many natural products,<sup>4</sup> medicinally relevant substances<sup>5</sup> and organic materials.<sup>6</sup> Amongst these nitrogen containing compounds, carbazoles, isolated first from coal tar in 1872 by Graebe and Glazer<sup>7</sup> are important class of hetero-aromatics and are embedded in several pharmaceuticals<sup>8</sup> as well as materials<sup>9</sup> with broad range of activities.<sup>10</sup> Therefore, in recent years synthesis of

carbazoles has remained as an active area of research. Alternatively, a variety of natural and non-natural products contain the pyran ring system in their structures.<sup>11</sup> To this end, a number of synthetic strategies to these targets have been reported.<sup>12</sup> In view of the various aplications of carbazoles as well as pyran-ring containing natural products, we are interested in assembling diverse and intricate hybrid molecules containing both of these subunits in a diversity-oriented manner under operationally simple reaction conditions involving minimum number of steps. The structures of some natural products containing pyrano-carbazole scaffold are shown in Fig. 1.<sup>13</sup>



Fig. 1. List of diverse bio-active pyrano-carbazole natural products

The retrosynthetic approach towards the synthesis of diverse pyrano-carbazole derivatives is shown in the Fig. 2. To this end, the target carbazole derivative **9** can be obtained from the enones **8** by employing FI followed by the Suzuki–Miyaura cross-coupling reaction. The enone derivatives **8** could be obtained from the cyclohaxane-1,3-dione derivatives **7a-c** *via* hetero-Diels–Alder reaction with different styrenes and paraformaldehyde under mild reaction conditions.





#### 2. Results and discussion

A general outline for the synthesis of diverse carbazole derivatives is shown in Scheme 1 and the structures of 1,3-diones as well as styrenes used in our study are shown in Fig. 3.

Our journey towards the synthesis of diverse and intricate pyrano-carbazole derivatives began with the preparation of the pyran derivative **8a** through the hetero-Diels–Alder reaction of styrene **11a** and paraformaldehyde **12** in glycerol by following the known procedure.<sup>14</sup> Here, we found that formation of the side product **14** (Scheme 2) was unavoidable and also we were unable to obtain the expected product in good yield (Table 1 and Entry 1). Therefore, we investigated various reaction conditions to avoid the formation of the side product **14** and to improve the yield of the desired product **8a** (Table 1). Later, the optimized reaction conditions were employed to other diones and styrenes to assemble a variety of pyrano-intermediates **8b-i** and **15a-c** in fair to excellent yields (Fig. 4).



Scheme 1. General scheme for the formation of pyrano-carbazoles



Fig. 3. List of 1,3-diones and styrene derivatives used in our study



Scheme 2. Synthesis of pyrano-enone intermediate 8a

Table 1: Optimization studies for the synthesis of compound 8a

Entry	Solvent	Temp.	Time	<b>8a</b> (% yield) <sup>a</sup>	14 (% yield)
1	glycerol	120 °C	16 h	57	14

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2	benzene	80 °C	24 h	<5	25
3	toluene	110 °C	24 h	13	28
4	xylene	120 °C	24 h	<10	46
5	1,4-dioxane	100 °C	15 h	82	-
6	DMSO	110 °C	16 h	59	<10
7	Et <sub>3</sub> N	90 °C	18 h	66	<10
8	triethylaminoethanol	110 °C	30 h	30	15
9	DMF	<b>110</b> °C	12 h	88	-
10	THF	66 °C	30 h	12	33
11	DMU:L-(+)TA (70:30)	80 °C	24 h/40 h	trace	-
12	DMU:L-(+)TA (50:50)	80 °C	24 h	trace	-

a= Isolated yields after column chromatography technique, DMU = 1,3-dimethyl urea, TA = tartaric acid



Fig. 4. List of pyrano-ketone intermediates assembled in our strategy

Having the ketone precursors **8a-f** in hand, our next target was to generate diverse pyranocarbazole derivatives *via* FI. To this end, survey of the literature indicated that the FI of  $\alpha$ ,  $\beta$ unsaturated carbonyl compounds *via* conventional protocol is not explored. Therefore, it remained a challenge to perform the FI of  $\alpha$ , $\beta$ -unsaturated carbonyl compounds by using conventional conditions. In this regard, the keto derivative **8a** was subjected to the FI with phenylhydrazine hydrochloride under different reaction conditions but in most of the cases, we realized low yield of the desired product (Table 2). The low yield and longer reaction time for the FI may be because of the reduction of electrophilicity of the carbonyl carbon due to

the conjugation of lone pair of the oxygen atom present in the ring system (Fig. 5). Therefore, the tendency of phenylhydrazine to attack the carbonyl group is decreased. After screening various reaction conditions to FI of 8a, we observed that *p*-toluene sulfonic acid (*p*-TSA) in refluxing toluene gave the expected product in a respectable yield (Table 2 and Entry 2). Later, the optimized reaction conditions were applied to other substrates to generate the desired products 13b-13k in moderate to good yields (Fig. 6).



Fig. 5. Resonating structures of keto precursor 8



Scheme 3. Synthesis of pyrano-carbazole 13a via FI

<b>Fable 2:</b> Optimization for the syn	thesis of pyrano-carbazole derivative 13	3a
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Entry	Solvent	Acid	Temp.	Time	<b>13a</b> (% yield) <sup>a</sup>
1	DMU:L-(+)-	TA (70:30)	75-80 °C	24 h	30
2	toluene	<i>p</i> -TSA	110 °C	3 days	69
3	toluene	CH <sub>3</sub> SO <sub>3</sub> H	110 °C	24 h	38
4	DMF	CH <sub>3</sub> SO <sub>3</sub> H	120 °C	24 h	53
5	toluene	HCl	110 °C	3 days	33
6	EtOH	$SOCl_2$	110 °C	3 days	<5
7	DMF	CH <sub>3</sub> SO <sub>3</sub> H	120 °C/MW	4 h	21
8	CH <sub>3</sub> COOH		110 °C	5 days	<10
9	CH <sub>3</sub> COOH	TFA	110 °C	3 days	18
10	DMF	CH <sub>3</sub> SO <sub>3</sub> H	120 °C*	36 h	46
11	toluene	PTSA	120 °C*	36 h	25
12	toluene	PPA	120 °C	24 h	NR

a = yields are based on starting material recovery; \*= Sealed tube; NR = no reaction, MW = microwave



Fig. 6. List of highly diversified pyrano-carbazole derivatives

To further expand the substrate scope of this methodology, the Suzuki–Miyaura crosscoupling reaction was employed with different boronic acids to generate diverse and highly functionalized pyrano-carbazole derivatives. In this context, we first performed the Suzuki-Miyaura cross-coupling reaction of compound **13f** with phenyl boronic acid to furnish the cross-coupling product **9a** in 94% yield (Scheme 4 and Fig. 7). Later, the coupling products **9b-d** were also prepared by using different boronic acid in good to excellent yields (Fig. 7).



Scheme 4. Synthesis of highly diversified pyrano-carbazole derivatives



Fig. 7. List of highly diversified pyrano-carbazole derivatives via Suzuki coupling

#### 3. Conclusions

In summary, we have demonstrated a very simple strategy to diverse and intricate pyranocarbazole derivatives under simple reaction conditions with minimum number of steps and without the involvement of protecting groups.<sup>15</sup> Here, we have used readily available starting 1,3-diones and styrenes to generate architecturally complex carbazoles which otherwise would be difficult to synthesize. The carbazole derivatives synthesized here resembles with natural products (Fig. 1) and this strategy may be useful for the construction of diverse natural products as well as boiactive targets.

#### 4. Experimental section

All commercially accessible reagents were used without further purification and the reactions involving air sensitive catalysts or reagents were performed in degassed solvents. Moisture sensitive materials were transferred by using syringe-septum techniques and the reactions were maintained under nitrogen atmosphere. Analytical thin layer chromatography (TLC) was performed on  $(7.5\times2.5 \text{ cm})$  glass plates coated with Acme's silica gel GF 254 (containing 13% calcium sulfate as a binder) by using a suitable mixture of EtOAc and petroleum ether for development. Column chromatography was performed by using Acme's silica gel (100-200 mesh) with an appropriate mixture of EtOAc and petroleum ether. The coupling constants (*J*) are given in hertz (Hz) and chemical shifts are denoted in parts per million (ppm) downfield from internal standard, tetramethylsilane (TMS). The abbreviations, s, d, t, q, m, dd and td, refer to singlet, doublet, triplet, quartet, multiplet, doublet of doublets, and triplet of doublets respectively. Infrared (IR) spectra were recorded on Nicolet Impact-400 FT IR spectrometer. Proton nuclear magnetic resonance (<sup>13</sup>C NMR, 100 MHz and 125 MHz) spectra were recorded on a Bruker spectrometer. The high-resolution mass measurements

were carried out by using electrospray ionization (ESI, Q-ToF) spectrometer. Melting points were recorded on a Veego melting point apparatus.

General procedure for the synthesis of 8a-i and 15a-c: The solution of compounds 7a-c or 10, formaldehyde 12 (2 equiv) and styrenes 11 (1.2 equiv) in DMF was heated at 110 °C for 10-18 h. At the conclusion of the reaction (TLC monitoring), the reaction mixture was diluted with water and the organic layer was extracted with EtOAc. Later, the organic layer was washed with water (4×50 mL) to remove the excess amount of DMF and the solvent was removed under reduced pressure. The crude products were purified by silica gel column chromatography (25% EtOAc-petroleum ether) to afford the desired products (Fig. 4).

General procedure for the synthesis of 13a-k: The solution of compounds 8a-f and *p*-TSA (5 equiv) in toluene was heated at 110 °C for 3-5 days. At the conclusion of the reaction (TLC monitoring), the reaction mixture was diluted with saturated aq. NaHCO<sub>3</sub> (10 mL) solution and the compounds were extracted with EtOAc. Solvent was removed under reduced pressure and the crude products were purified by silica gel column chromatography by using appropriate mixtures of EtOAc-petroleum ether to afford the expected products (Fig. 6).

General procedure for the Suzuki–Miyaura cross-coupling of 13f and 13k: To a solution of bromo derivatives 13f or 13k in THF/toluene/water (1:1:1, each 10 mL), were added Na<sub>2</sub>CO<sub>3</sub> (3.0 equiv) and arylboronic acid (2.0 equiv). The reaction mixture was degassed with nitrogen for 15 min. Later, Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) was added and the reaction mixture was heated at 100 °C. At the conclusion of the reaction (TLC monitoring), the reaction mixture was diluted with water and the organic layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The solvent was removed under reduced pressure and the crude products were purified by silica gel column chromatography by using appropriate mixtures of EtOAc-petroleum ether to afford the desired cross-coupling products (Fig. 7).

**2-Phenyl-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8a:** Thick colourless liquid; yield = 88% (896 mg, starting from 500 mg of **7a**); reaction time = 10 h;  $R_f = 0.40$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.84$ -1.96 (m, 3H), 2.09-2.15 (m, 1H), 2.20-2.31 (m, 1H), 2.34-2.44 (m, 5H), 4.90 (dd,  $J_1 = 2.40$  Hz,  $J_2 = 10.40$  Hz, 1H), 7.27-7.37 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 18.1$ , 20.9, 28.6, 29.1, 36.6, 78.9, 111.6, 125.8, 128.1, 128.5, 140.2, 171.4, 198.1; IR (neat):  $v_{max} = 1266$ , 1602, 1659, 2855, 2926, 3074 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>15</sub>H<sub>17</sub>O<sub>2</sub> [M+H]<sup>+</sup> 229.1223, found: 229.1222.

**2-(4-Fluorophenyl)-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8b:** White solid; yield = 81% (889 mg, starting from 500 mg of **7a**); reaction time = 16 h; mp 69-71 °C;  $R_f = 0.41$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.80$ -1.91 (m, 2H), 1.97-2.03 (m, 2H), 2.12-2.17 (m, 1H), 2.23-2.31 (m, 1H), 2.39-2.47 (m, 4H), 4.91 (dd,  $J_1 = 1.96$  Hz,  $J_2 = 10.48$  Hz, 1H), 7.05-7.09 (m, 2H), 7.30-7.34 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 18.4$ , 21.1, 28.8, 29.4, 36.8, 78.6, 111.8, 115.6, 115.8, 127.8, 127.9, 136.2, 136.3, 162.7 (d, J = 245.0 Hz), 171.6, 198.4; IR (neat):  $v_{max} = 1647$ , 2867, 2949, 3054 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>15</sub>H<sub>15</sub>FNaO<sub>2</sub> [M+Na]<sup>+</sup> 269.0948, found: 269.0948.

**2-(4-Bromophenyl)-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8c:** White solid; yield = 80% (1.13 g, starting from 500 mg of **7a**); reaction time = 16 h; mp 94-97 °C;  $R_f = 0.38$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.77$ -1.89 (m, 2H), 1.96-2.03 (m, 2H), 2.11-2.17 (m, 1H), 2.22-2.31 (m, 1H), 2.38-2.47 (m, 4H), 4.89 (dd,  $J_1 = 2.22$  Hz,  $J_2 = 10.44$  Hz, 1H), 7.22 (d, J = 8.44 Hz, 2H), 7.49-7.53 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 18.2$ , 21.0, 28.8, 29.3, 36.8, 78.5, 111.9, 122.2, 127.8, 131.9, 139.5, 171.3, 198.3; IR (neat):  $v_{max} = 1394$ , 1489, 1620, 1644, 2945, 3052 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>15</sub>H<sub>15</sub><sup>79</sup>BrNaO<sub>2</sub> [M+Na]<sup>+</sup> 329.0148, found: 329.0156.

**2,7-Diphenyl-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8d:** Thick yellow liquid of an inseparable mixture of diastereomers (0.5:1); yield = 82% (663 mg, starting from 500 mg of **7b**); reaction time = 15 h;  $R_f = 0.46$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) for major diastereomer with some peaks overlapping:  $\delta = 1.90-1.98$  (m, 1H), 2.17-2.23 (m, 1H), 2.29-2.37 (m, 1H), 2.42-2.48 (m, 1H), 2.60-2.84 (m, 4H), 3.38-3.46 (m, 1H), 5.10 (dd,  $J_I = 2.70$  Hz,  $J_2 = 9.50$  Hz, 1H), 7.31-7.40 (m, 10H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) for both diastereomers:  $\delta = 17.5$ , 18.6, 28.7, 29.4, 36.2, 36.3, 39.0, 39.1, 43.8, 43.9, 79.2, 79.6, 111.4, 111.6, 125.9, 126.1, 126.7, 126.8, 127.0, 127.1, 128.3, 128.4, 128.7, 128.8, 128.9, 140.2, 140.3, 143.0, 143.1, 170.5, 170.8, 197.1, 197.4; IR (neat):  $v_{max} = 1399$ , 1496, 1623, 1652, 2942, 3064 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>21</sub>H<sub>21</sub>O<sub>2</sub> [M+H]<sup>+</sup> 305.1536, found: 305.1539.

2-(4-Fluorophenyl)-7-phenyl-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8e: Thick yellow liquid of an inseparable mixture of diastereomers; yield = 73% (625 mg, starting from 500 mg of 7b); reaction time = 18 h;  $R_f$  = 0.45 (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) for major diastereomer with some peaks overlapping:  $\delta$  = 1.86-1.91 (m, 1H), 2.14-2.18 (m, 1H), 2.29-2.33 (m, 1H), 2.43-57 (m, 1H), 2.60-2.80 (m, 4H), 3.36-3.43 (m, 1H), 5.04 (dd,  $J_1$  = 2.40 Hz,  $J_2$  = 9.65 Hz, 1H), 7.02-7.08 (m, 2H), 7.23-7.34 (m, 7H); <sup>13</sup>C

NMR (125 MHz, CDCl<sub>3</sub>) for both diastereomers:  $\delta = 17.5$ , 18.6, 28.7, 29.4, 36.2, 36.3, 38.9, 39.1, 43.7, 43.8, 78.6, 78.9, 111.4, 111.6, 115.5, 115.7, 126.7, 126.8, 127.0, 127.1, 127.6, 127.7, 127.8, 127.9, 128.8, 128.9, 136.0, 136.0, 136.1, 142.9, 143.0, 162.6 (d, J = 196.0 Hz) 162.7 (d, J = 196.0 Hz), 170.4, 170.6, 197.1, 197.3; IR (neat):  $v_{max} = 1394$ , 1512, 1624, 1652, 2857, 2947, 3030 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>21</sub>H<sub>19</sub>FNaO<sub>2</sub> [M+Na]<sup>+</sup> 345.1261, found: 345.1264.

**2-(4-Bromophenyl)-7-phenyl-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8f:** White solid of an inseparable mixture of diastereomers; yield = 72% (1.46 g, starting from 500 mg of **7b**); reaction time = 16 h; mp 147-150 °C;  $R_f$  = 0.45 (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) for major diastereomer with some peaks overlapping:  $\delta$  = 1.83-1.91 (m, 1H), 2.13-2.19 (m, 1H), 2.26-2.33 (m, 1H), 2.40-58 (m, 1H), 2.60-2.81 (m, 4H), 3.36-3.44 (m, 1H), 5.03 (dd,  $J_1$  = 2.55 Hz,  $J_2$  = 9.50 Hz, 1H), 7.17 (d, J = 10.00 Hz, 1H), 7.22-7.25 (m, 4H), 7.33 (t, J = 7.85 Hz, 2H), 7.48-7.52 (m, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) for both diastereomers:  $\delta$  = 17.5, 18.6, 28.7, 29.5, 36.3, 36.3, 39.0, 39.2, 43.8, 43.9, 78.5, 78.8, 111.5, 111.7, 122.2, 122.3, 126.8, 126.9, 127.1, 127.2, 127.6, 127.8, 128.9, 129.0, 131.9, 139.3, 139.3, 142.9, 143.0, 170.3, 170.5, 197.1, 197.4; IR (neat):  $v_{max}$  = 1266, 1393, 1491, 1625, 1649, 2955, 3055 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m*/*z*: calculated for C<sub>21</sub>H<sub>19</sub><sup>79</sup>BrNaO<sub>2</sub> [M+Na]<sup>+</sup> 405.0461, found: 405.0461.

**7,7-Dimethyl-2-phenyl-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8g:** Creamy solid; yield = 93% (850 mg, starting from 500 mg of **7c**); reaction time = 12 h; mp 99-101 °C;  $R_f = 0.43$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.07$  (d, J = 7.28 Hz, 6H), 1.84-1.90 (m, 1H), 2.13-2.17 (m, 1H), 2.22-2.34 (m, 5H), 2.43 (d, J = 16.48 Hz, 1H), 4.94 (dd,  $J_I = 1.92$  Hz,  $J_2 = 10.12$  Hz, 1H), 7.27-7.39 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 17.8$ , 27.7, 29.1, 29.2, 32.1, 42.4, 50.6, 79.0, 110.3, 125.9, 126.09, 128.2, 128.4, 128.6, 140.3, 169.7, 197.9; IR (neat):  $v_{max} = 1451$ , 1630, 1647, 2954, 3027 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>17</sub>H<sub>20</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup> 279.1356, found: 279.1355.

**2-(4-Fluorophenyl)-7,7-dimethyl-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8h:** Creamy solid; yield = 85% (832 mg, starting from 500 mg of **7c**); reaction time = 12 h; mp 101-106 °C;  $R_f = 0.43$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 1.09$  (d, J = 7.20 Hz, 6H), 1.83-1.92 (m, 1H), 2.11-2.22 (m, 1H), 2.24-2.36 (m, 5H), 2.46 (d, J = 16.60 Hz, 1H), 4.94 (d, J = 10.35 Hz, 1H), 7.05-7.08 (m, 2H), 7.29-7.33 (m, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 17.9$ , 27.7, 29.1, 29.2, 32.1, 42.4, 50.6, 78.4, 110.3, 115.4, 115.6, 127.7, 127.8, 136.1, 136.2, 162.5 (d, J = 196.0 Hz), 169.6, 197.9; IR (neat):  $v_{max} = 1268$ ,

1350, 1649, 2953, 3020 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>17</sub>H<sub>19</sub>FNaO<sub>2</sub> [M+Na]<sup>+</sup> 297.1261, found: 297.1264.

**2-(4-Bromophenyl)-7,7-dimethyl-2,3,4,6,7,8-hexahydro-5H-chromen-5-one 8i:** Brown solid; yield = 87% (1.03 g, starting from 500 mg of **7c**); reaction time = 13 h; mp 144-145 °C;  $R_f = 0.44$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.08$  (d, J = 7.25 Hz, 6H), 1.78-1.88 (m, 1H), 2.11-2.18 (m, 1H), 2.21-2.33 (m, 5H), 2.41-2.47 (m, 1H), 4.92 (dd,  $J_1 = 2.40$  Hz,  $J_2 = 10.24$  Hz, 1H), 7.20-7.22 (m, 2H), 7.49-7.52 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 17.8$ , 27.8, 29.2, 29.3, 32.2, 42.5, 50.7, 78.4, 110.5, 122.2, 127.7, 131.9, 139.5, 169.6, 198.0; IR (neat):  $v_{max} = 1621$ , 1645, 2871, 2944, 3050 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>17</sub>H<sub>19</sub><sup>79</sup>BrNaO<sub>2</sub> [M+Na]<sup>+</sup> 357.0461, found: 357.0462.

**2-Phenyl-3,4-dihydroindeno[1,2-b]pyran-5(2H)-one 15a:** Sticky yellow liquid; yield = 42% (377 mg, starting from 500 mg of **10**); reaction time = 12 h;  $R_f = 0.42$  (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 2.01$ -2.09 (m, 1H), 2.20-2.27 (m, 1H), 2.35-2.46 (m, 2H), 5.27 (dd,  $J_I = 2.48$  Hz,  $J_2 = 9.92$  Hz, 1H), 7.12 (d, J = 7.08 Hz, 1H), 7.23-7.31 (m, 2H), 7.36-7.45 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 16.4$ , 29.5, 81.7, 108.2, 117.7, 121.1, 126.1, 128.6, 128.8, 129.9, 132.0, 133.5, 138.2, 139.6, 174.5, 193.3; IR (neat):  $v_{max} = 1283$ , 1594, 1631, 1695, 2851, 2927, 3063 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>18</sub>H<sub>14</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup> 285.0886, found: 285.0885.

**2-(4-Fluorophenyl)-3,4-dihydroindeno[1,2-b]pyran-5(2H)-oned 15b:** Sticky yellow liquid; yield = 34% (326 mg, starting from 500 mg of **10**); reaction time = 15 h;  $R_f$  = 0.44 (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.96-2.06 (m, 1H), 2.19-2.25 (m, 1H), 2.36-2.46 (m, 2H), 5.25 (dd,  $J_I$  = 2.12 Hz,  $J_2$  = 10.08 Hz, 1H), 7.04-7.14 (m, 3H), 7.23-7.31 (m, 2H), 7.37-7.41 (m, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 16.5, 29.5, 81.1, 108.2, 115.7, 115.9, 117.7, 121.2, 128.0, 128.1, 129.9, 132.0, 133.4, 135.5, 135.5, 138.1, 162.9 (d, J = 246.0 Hz), 174.4, 193.3; IR (neat):  $v_{max}$  = 1475, 2846, 2923, 3043 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>18</sub>H<sub>14</sub>FO<sub>2</sub> [M+H]<sup>+</sup> 281.0972, found: 281.0974.

**2-(4-Bromophenyl)-3,4-dihydroindeno[1,2-b]pyran-5(2H)-one 15c:** Sticky yellow liquid; yield = 33% (154 mg, starting from 200 mg of **10**); reaction time = 12 h;  $R_f$  = 0.40 (silica gel, 25% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.93-2.01 (m, 1H), 2.17-2.22 (m, 1H), 2.37-2.41 (m, 2H), 5.20 (dd,  $J_1$  = 2.24 Hz,  $J_2$  = 10.05 Hz, 1H), 7.09 (d, J = 6.80 Hz, 1H), 7.22-7.29 (m, 4H), 7.37 (dd,  $J_1$  = 0.75 Hz,  $J_2$  = 6.35 Hz, 1H), 7.52-7.54 (m, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 16.3, 29.4, 80.9, 108.2, 117.7, 121.2, 122.5, 127.8, 129.9,

131.9, 132.0, 133.3, 138.0, 138.6, 174.2, 193.2; IR (neat):  $v_{max} = 1394$ , 2829, 2955, 3020 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>18</sub>H<sub>14</sub><sup>79</sup>BrO<sub>2</sub> [M+H]<sup>+</sup> 341.0177, found: 341.0176. **3-Phenyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13a:** White solid; yield = 69% (90 mg, starting from 100 mg of **8a**); reaction time = 3 days; mp 216-217 °C;  $R_f = 0.52$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 2.19-2.27$  (m, 1H), 2.33-2.37 (m, 1H), 2.89 (d, J = 13.25 Hz, 1H), 3.01-3.07 (m, 1H), 5.12 (d, J = 10.10 Hz, 1H), 6.87 (d, J = 8.45 Hz, 1H), 7.21 (t, J = 7.70 Hz, 1H), 2.24-2.35 (m, 2H), 7.39-7.42 (m, 3H), 7.47 (d, J = 7.30 Hz, 2H), 7.81 (d, J = 8.50 Hz, 2H), 7.97 (d, J = 7.70 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 20.7$ , 29.4, 77.8, 104.1, 110.3, 110.6, 116.6, 119.1, 119.7, 119.8, 124.3, 124.4, 126.3, 128.1, 128.7, 139.2, 139.5, 141.7, 154.0; IR (neat):  $v_{max} = 1535$ , 2857, 2987, 3023, 3444 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>21</sub>H<sub>18</sub>NO [M+H]<sup>+</sup> 300.1383, found: 300.1389.

**11-Methyl-3-phenyl-1,2,3,11-tetrahydropyrano**[**3,2-a**]**carbazole 13b:** White solid; yield = 57% (125 mg, starting from 200 mg of **8a**, starting material recovered = 40 mg); reaction time = 4 days; mp 193-195 °C;  $R_f = 0.63$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 2.05-2.15$  (m, 1H), 2.26-2.30 (m, 1H), 3.36-3.43 (m, 2H), 3.98 (s, 3H), 5.06 (d, J = 8.36, 1H), 6.79 (d, J = 8.40, 1H), 7.13 (t, J = 7.36 Hz, 1H), 7.18-7.42 (m, 7H), 7.75 (d, J = 8.44 Hz, 1H), 7.89 (d, J = 7.64 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 23.1$ , 29.9, 32.8, 77.1, 105.1, 108.5, 110.6, 117.2, 119.2, 119.3, 123.4, 124.3, 126.2, 128.0, 128.7, 140.4, 141.8, 141.9, 154.6; IR (neat):  $v_{max} = 1463$ , 1592, 2920, 3040 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>22</sub>H<sub>20</sub>NO [M+H]<sup>+</sup> 314.1539, found: 314.1537.

**3-(4-Fluorophenyl)-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13c:** White solid; yield = 43% (40 mg, starting from 100 mg of **8b**, starting material recovered = 28 mg); reaction time = 3 days; mp 210-212 °C;  $R_f$  = 0.55 (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.16-2.24 (m, 1H), 2.30-2.35 (m, 1H), 2.88-2.92 (m, 1H), 30.1-3.07 (m, 1H), 5.10 (dd,  $J_I$  = 2.00 Hz,  $J_2$  = 10.25 Hz, 1H), 6.86 (d, J = 8.45 Hz, 1H), 7.08-7.12 (m, 2H), 7.21-7.24 (m, 1H), 7.32-7.35 (m, 1H), 7.40-7.47 (m, 3H), 7.82 (d, J = 8.45 Hz, 1H), 7.87 (brs, 1H), 7.98 (d, J = 7.70 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 20.7, 29.5, 77.4, 104.0, 110.3, 110.7, 115.5, 115.6, 116.7, 119.2, 119.7, 119.9, 124.2, 124.5, 127.9, 128.0, 137.5, 137.5, 139.2, 139.6, 153.9, 162.6 (d, J = 196.0 Hz); IR (neat):  $v_{max}$  = 1266, 1456, 1593, 1605, 2855, 2929, 3045, 3387 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>21</sub>H<sub>16</sub>FNNaO [M+Na]<sup>+</sup> 340.1108, found: 340.1108.

**3-(4-Fluorophenyl)-11-methyl-1,2,3,11-tetrahydropyrano**[**3,2-a**]**carbazole 13d:** White solid; yield = 61% (53 mg, starting from 100 mg of **8b**, starting material recovered = 35 mg); reaction time = 4 days; mp 190-192 °C;  $R_f = 0.53$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 2.04$ -2.15 (m, 1H), 2.27-2.30 (m, 1H), 3.40-3.44 (m, 2H), 4.01 (s, 3H), 5.05 (d, J = 10.16 Hz, 1H), 6.82 (d, J = 8.44 Hz, 1H), 7.07 (t, J = 8.68 Hz, 2H), 7.18-7.24 (m, 1H), 7.28 (d, J = 8.12 Hz, 1H), 7.35-7.44 (m, 3H), 7.81 (d, J = 8.44 Hz, 1H), 7.95 (d, J = 7.68 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 23.1$ , 30.0, 32.7, 76.8, 105.0, 108.5, 110.5, 115.4, 115.6, 117.3, 119.2, 119.2, 119.3, 123.3, 124.3, 127.9, 128.0, 137.5, 137.6, 140.3, 141.9, 154.4, 162. 6 (d, J = 244.0 Hz); IR (neat):  $v_{max} = 1347$ , 1563, 1597, 2861, 3010 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m*/*z*: calculated for C<sub>22</sub>H<sub>19</sub>FNO [M+H]<sup>+</sup> 332.1445, found: 332.1447.

**3-(4-Bromophenyl)-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13e:** White solid; yield = 42% (197 mg, starting from 500 mg of **8c**, starting material recovered = 120 mg); reaction time = 4 days; mp 235-237 °C;  $R_f = 0.50$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 2.05-2.25$  (m, 1H), 2.32-2.38 (m, 1H), 2.89-2.95 (m, 1H), 3.02-3.11 (m, 1H), 5.10 (dd,  $J_I = 2.04$  Hz,  $J_2 = 10.12$  Hz, 1H), 6.86 (d, J = 8.44 Hz, 1H), 7.07 (t, J = 8.68 Hz, 2H), 7.31-7.37 (m, 3H), 7.41 (d, J = 8.00 Hz, 1H), 7.53 (d, J = 8.40 Hz, 1H), 7.83 (d, J = 8.56 Hz, 2H), 7.97 (d, J = 7.68 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 20.6$ , 29.4, 77.0, 103.9, 110.2, 110.6, 116.7, 119.2, 119.7, 119.9, 121.9, 124.2, 124.5, 127.9, 131.8, 139.1, 139.5, 140.7, 153.7; IR (neat):  $v_{max} = 1070$ , 1266, 1459, 1608, 2928, 3057, 3447 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>21</sub>H<sub>17</sub><sup>79</sup>BrNO [M+H]<sup>+</sup> 378.0488, found: 378.0483.

**3-(4-Bromophenyl)-11-methyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13f**: White solid; yield = 50% (48 mg, starting from 100 mg of **8**c, starting material recovered = 24 mg); reaction time = 5 days; mp 222-225 °C;  $R_f = 0.53$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 2.05-2.16$  (m, 1H), 2.30-2.34 (m, 1H), 3.41-3.52 (m, 2H), 4.06 (s, 3H), 5.08 (dd,  $J_I = 1.80$  Hz,  $J_2 = 10.00$  Hz, 1H), 6.84 (d, J = 8.40 Hz, 1H), 7.21 (t, J = 7.60 Hz, 1H), 7.31-7.41 (m, 4H), 7.53 (d, J = 8.40 Hz, 2H), 7.83 (d, J = 8.45 Hz, 1H), 7.96 (d, J = 7.70 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 22.9$ , 29.9, 32.8, 76.9, 105.0, 108.6, 110.5, 117.3, 119.2, 119.3, 119.3, 121.8, 123.3, 124.4, 127.9, 131.8, 140.3, 140.8, 141.9, 154.2; IR (neat):  $v_{max} = 1247$ , 1443, 1593, 2855, 2929, 3025 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>22</sub>H<sub>19</sub><sup>79</sup>BrNO [M+H]<sup>+</sup> 392.0649, found: 392.0656.

**3,6-Diphenyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13g:** Yellow solid; yield = 63% (33 mg, starting from 100 mg of **8d**, starting material recovered = 58 mg); reaction time = 4

days; mp 201-203 °C;  $R_f = 0.50$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 2.23$ -2.29 (m, 1H), 2.35-2.40 (m, 1H), 2.91-2.96 (m, 1H), 3.03-3.12 (m, 1H), 5.15 (dd,  $J_I = 2.08$  Hz,  $J_2 = 10.08$  Hz, 1H), 6.81 (s, 1H), 6.97 (t, J = 7.88 Hz, 1H), 7.25-7.29 (m, 2H), 7.33-7.53 (m, 10H), 7.63 (d, J = 7.15 Hz, 1H), 7.98 (brs, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 20.6$ , 29.5, 77.8, 102.9, 110.5, 111.6, 114.2, 119.4, 121.7, 123.9, 124.3, 126.2, 127.6, 128.0, 128.5, 128.7, 128.8, 129.3, 136.8, 139.5, 139.8, 141.0, 141.6, 153.6; IR (neat):  $v_{max} = 1274$ , 1459, 1588, 1618, 2850, 2925, 3057, 3409 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>27</sub>H<sub>22</sub>NO [M+H]<sup>+</sup> 376.1696, found: 376.1695.

**11-Methyl-3,6-diphenyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13h:** Brown solid; yield = 48% (162 mg, starting from 300 mg of **8d**, starting material recovered = 36 mg); reaction time = 3 days; mp 184-185 °C;  $R_f$  = 0.65 (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.17-2.25 (m, 1H), 2.36-2.41 (m, 1H), 3.51-3.56 (m, 2H), 4.10 (s, 3H), 5.17 (dd,  $J_I$  = 1.84 Hz,  $J_2$  = 10.00 Hz, 1H), 6.77 (s, 1H), 6.90-6.94 (m, 1H), 7.25 (t, J = 3.88 Hz, 2H), 7.31 (d, J = 3.80 Hz, 2H), 7.34 (d, J = 7.24 Hz, 1H), 7.41 (t, J = 7.12 Hz, 2H), 7.45-7.50 (m, 4H), 7.58 (d, J = 6.64 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 23.3, 30.1, 32.9, 77.1, 104.0, 108.4, 112.1, 114.9, 118.9, 121.5, 123.0, 124.2, 126.2, 127.6, 128.0, 128.5, 128.7, 129.3, 136.9, 140.9, 141.1, 141.8, 142.3, 154.1; IR (neat):  $v_{max}$  = 1266, 1568, 1584, 2854, 2924, 3050 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>28</sub>H<sub>24</sub>NO [M+H]<sup>+</sup> 390.1852, found: 390.1851.

**3-(4-Fluorophenyl)-11-methyl-6-phenyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13i:** Yellow solid; yield = 68% (40 mg, starting from 100 mg of **8e**, starting material recovered = 53 mg); reaction time = 4 days; mp 198-200 °C;  $R_f$  = 0.69 (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.13-2.29 (m, 1H), 2.35-2.39 (m, 1H), 3.51-3.55 (m, 2H), 4.10 (s, 3H), 5.15 (d, *J* = 8.84 Hz, 1H), 6.79 (s, 1H), 6.95-6.99 (m, 1H), 7.14 (t, *J* = 8.64 Hz, 2H), 7.29-7.38 (m, 3H), 7.47-7.56 (m, 5H), 7.62 (d, *J* = 7.12 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 23.3, 30.1, 32.9, 76.8, 103.9, 108.4, 112.0, 114.9, 115.4, 115.6, 119.0, 121.4, 122.9, 124.2, 127.6, 127.8, 127.9, 128.5, 129.3, 136.9, 137.5, 137.5, 140.8, 141.1, 142.2, 153.9, 162.6 (d, *J* = 244.0 Hz); IR (neat):  $v_{max}$  = 1289, 1388, 1467, 1583, 2850, 2923, 3054 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m*/*z*: calculated for C<sub>28</sub>H<sub>23</sub>FNO [M+H]<sup>+</sup> 408.1758, found: 408.1757.

**3-(4-Bromophenyl)-6-phenyl-1,2,3,11-tetrahydropyrano**[**3,2-a**]**carbazole 13j:** White solid; yield = 63% (149 mg, starting from 200 mg of **8f**); reaction time = 3 days; mp 273-274 °C;  $R_f = 0.53$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta =$ 

2.09-2.12 (m, 1H), 2.25-2.26 (m, 1H), 2.81-2.83 (m, 1H), 2.96-2.98 (m, 1H), 5.02 (d, J = 9.70 Hz, 1H), 6.72 (s, 1H), 6.90 (t, J = 7.40 Hz, 1H), 7.16-7.22 (m, 1H), 7.28-7.31 (m, 3H), 7.36-7.51 (m, 6H), 7.56 (d, J = 7.10 Hz, 2H), 7.85 (brs, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 20.5$ , 29.4, 77.1, 102.8, 110.5, 111.5, 114.3, 119.5, 121.7, 121.9, 123.8, 124.4, 127.6, 127.9, 128.5, 129.3, 131.8, 136.9, 139.4, 139.8, 140.7, 140.9, 153.3; IR (neat):  $v_{max} = 1267$ , 1369, 1468, 1604, 2853, 2929, 3030, 3417 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>27</sub>H<sub>21</sub><sup>79</sup>BrNO [M+H]<sup>+</sup> 454.0807, found: 454.0809.

**3-(4-Bromophenyl)-11-methyl-6-phenyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 13k:** White solid; yield = 55% (104 mg, starting from 200 mg of **8**f, starting material recovered = 45 mg); reaction time = 5 days; mp 167-169 °C;  $R_f = 0.66$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 2.05-2.19$  (m, 1H), 2.37 (d, J = 13.35 Hz, 1H), 3.48-3.56 (m, 2H), 4.11 (s, 3H), 5.14 (d, J = 9.35 Hz, 1H), 6.75 (s, 1H), 6.91-6.94 (m, 1H), 7.27 (s, 2H), 7.32 (d, J = 3.75 Hz, 2H), 7.37 (d, J = 8.35 Hz, 2H), 7.46-7.58 (m, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 23.1$ , 30.0, 33.0, 76.9, 103.8, 108.4, 112.0, 115.1, 119.0, 121.5, 121.8, 123.0, 124.3, 127.6, 127.9, 128.5, 128.9, 129.3, 131.8, 137.0, 140.8, 141.1, 142.3, 153.8; IR (neat):  $v_{max} = 1468$ , 1598, 2813, 2924, 3054 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>28</sub>H<sub>23</sub><sup>79</sup>BrNO [M+H]<sup>+</sup> 468.0958, found: 468.0942.

**3-([1,1'-Biphenyl]-4-yl)-11-methyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazole 9a:** White solid; yield = 94% (23 mg, starting from 25 mg of **13f**); reaction time = 15 h; mp 254-258 °C;  $R_f = 0.55$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 2.00-2.25$  (m, 1H), 2.39-2.43 (m, 1H), 3.52-3.56 (m, 2H), 4.08 (s, 3H), 5.19 (d, J = 9.92 Hz, 1H), 6.78 (s, 1H), 6.89-6.93 (m, 1H), 7.247.34- (m, 3H), 7.42-7.54 (m, 4H), 7.57-7.64 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 23.3$ , 30.0, 32.9, 77.9, 104.0, 108.4, 112.1, 114.9, 119.0, 121.5, 123.0, 124.2, 126.7, 127.3, 127.5, 127.6, 128.5, 128.5, 129.3, 136.9, 140.8, 140.9, 141.0, 141.2, 142.3, 154.1; IR (neat):  $v_{max} = 1463$ , 1562, 2854, 2925, 3055 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>28</sub>H<sub>24</sub>NO [M+H]<sup>+</sup> 390.1852, found: 390.1855.

### 4'-(11-Methyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazol-3-yl)-[1,1'-biphenyl]-4-

**carbonitrile 9b:** White solid; yield = 86% (46 mg, starting from 50 mg of **13f**); reaction time = 24 h; mp 170 °C (decomposed);  $R_f = 0.52$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 2.19-2.24$  (m, 1H), 2.38-2.42 (m, 1H), 3.47-3.54 (m, 2H), 4.08 (s, 3H), 5.20 (dd,  $J_1 = 2.00$  Hz,  $J_2 = 10.01$  Hz, 1H), 6.87 (d, J = 8.45 Hz, 1H), 7.21 (dt,  $J_1 = 0.85$  Hz,  $J_2 = 7.10$  Hz, 1H), 7.33 (d, J = 8.15 Hz, 1H), 7.39 (dt,  $J_1 = 1.15$  Hz,  $J_2 = 8.20$  Hz, 1H), 7.59-7.64 (m, 4H), 7.69-7.75 (m, 4H), 7.85 (d, J = 8.45 Hz, 1H), 7.98 (d, J = 7.65 Hz, 1H), 7.99 (dt,  $J_2 = 7.65$  Hz, 1H), 7.99 (dt,  $J_3 = 7.65$  Hz, 1H), 7.99 (dt,  $J_4 = 7.65$  Hz, 1H), 7.90 (dt,  $J_4$ 

1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 23.0, 29.9, 32.8, 76.9, 105.0, 108.6, 110.5, 111.1, 117.3, 119.1, 119.2, 119.3, 119.4, 123.3, 124.4, 127.0, 127.6, 127.8, 132.8, 138.8, 140.3, 141.9, 142.4, 145.4, 154.4; IR (neat):  $v_{max}$  = 1247, 1363, 1443, 1466, 1593, 1605, 2225, 2854, 2924, 3054 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m*/*z*: calculated for C<sub>29</sub>H<sub>22</sub>N<sub>2</sub>NaO [M+Na]<sup>+</sup> 437.1624, found: 437.1623.

1-(4'-(11-Methyl-1,2,3,11-tetrahydropyrano[3,2-a]carbazol-3-yl)-[1,1'-biphenyl]-4-

yl)ethan-1-one 9c: White solid; yield = 90% (20 mg, starting from 20 mg of 13f); reaction time = 12 h; mp 212-215 °C;  $R_f = 0.43$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 2.16-2.23$  (m, 1H), 2.43-2.48 (m, 1H), 2.65 (s, 3H), 3.52-3.55 (m, 2H), 4.09 (s, 3H), 5.20 (d, J = 9.15 Hz, 1H), 6.87 (d, J = 8.35 Hz, 1H), 7.22 (t, J = 7.20 Hz, 1H), 7.33 (d, J = 8.05 Hz, 1H), 7.59 (t, J = 7.95 Hz, 1H), 7.59 (d, J = 8.07 Hz, 2H), 7.69 (dd,  $J_1 = 6.20$  Hz,  $J_2 = 14.20$  Hz, 4H), 7.84 (d, J = 8.35 Hz, 1H), 7.97 (d, J = 7.45 Hz, 1H), 8.04 (d, J = 8.15 Hz, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 23.0$ , 26.8, 29.9, 32.8, 76.9, 105.1, 108.6, 110.6, 117.3, 119.2, 119.3, 119.3, 123.4, 124.4, 126.9, 127.4, 127.6, 129.1, 136.1, 139.6, 140.4, 141.9, 145.6, 154.4, 197.9; IR (neat):  $v_{max} = 1259$ , 1509, 1598, 1706, 2857, 2926, 3069 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) m/z: calculated for C<sub>30</sub>H<sub>25</sub>NNaO<sub>2</sub> [M+Na]<sup>+</sup> 454.1777, found: 454.1775.

**3-(4'-Fluoro-[1,1'-biphenyl]-4-yl)-11-methyl-6-phenyl-1,2,3,11-tetrahydropyrano[3,2a]carbazole 9d:** White solid; yield = 82% (21 mg, starting from 25 mg of **13k**); reaction time

a jean ballofe solid, yield = 02/6 (21 mg, starting from 25 mg of 10k), reaction time = 15 h; mp 265-266 °C;  $R_f = 0.57$  (silica gel, 10% EtOAc-petroleum ether); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 2.23-2.29$  (m, 1H), 2.43-2.46 (m, 1H), 3.55-3.60 (m, 2H), 4.13 (s, 3H), 5.24 (dd,  $J_1 = 1.55$  Hz,  $J_2 = 10.00$  Hz, 1H), 6.81 (s, 1H), 6.94-6.98 (m, 1H), 7.14-7.18 (m, 2H), 7.30 (s, 1H), 7.34 (d, J = 3.20 Hz, 2H), 7.47-7.55 (m, 3H), 7.57-7.63 (m, 8H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 23.3$ , 30.0, 32.9, 76.9, 103.9, 108.4, 112.1, 114.9, 115.7, 115.9, 119.0, 121.5, 123.0, 124.2, 126.7, 127.3, 127.6, 128.5, 128.8, 128.8, 129.3, 136.9, 137.1, 137.1, 140.0, 140.8, 140.9, 141.1, 142.3, 154.0, 162.7 (d, J = 196.0 Hz); IR (neat):  $v_{max} =$ 1571, 1600, 2861, 2925, 3054 cm<sup>-1</sup>; HRMS (ESI, Q-ToF) *m/z*: calculated for C<sub>34</sub>H<sub>27</sub>FNO [M+H]<sup>+</sup> 484.2071, found: 484.2076.

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#### **Supplementary Information**

The copies of <sup>1</sup>H and <sup>13</sup>C NMR for all the new compounds associated with this article can be found at <u>http://dx.doi.org/</u>.....

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## **Supporting Information**

Diversity-oriented approach to natural product inspired pyrano-carbazole derivatives: Strategic utilization of hetero-Diels–Alder reaction, Fisher indolization and the Suzuki– Miyaura cross-coupling reaction

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