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Solvent-free synthesis of naphthopyrans under ball-milling conditions

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ABSTRACT

Under solvent-free ball-milling conditions, the nucleophilic addition reactions of terminal alkynes to carbonyl compounds promoted by KOH proceeded efficiently at ambient temperature. Subsequent cyclization reactions of the synthesized propargylic alcohols with 2-naphthol catalyzed by indium trichloride tetrahydrate, leading to the formation of naphthopyrans, were then investigated. In most cases, side reactions were avoided and thus high yields were achieved.

1. Introduction

The addition reactions of terminal alkynes to aldehydes and ketones are important processes in organic synthesis because of the formation of versatile propargylic alcohols.[1] Traditional process is carried out by using alkali or alkali earth metal (Na, Li, Mg)[2] alkynides or B, Al, Ce and V-alkynides[3] prepared from the transmetallation of alkali or alkali earth metal derivatives. These organometallic reagents are air-/water-sensitive and thus turn out to be of disadvantage. Several improved procedures for the alkynylations of aldehydes catalyzed by a Lewis acid in combination with a base have recently been reported.[4] More practically, there are several patents,[5] which are related to the use of potassium hydroxide as a base in liquid ammonia, a process referred to as the Favorskii reaction. Therefore, the reactions of alkynes with carbonyl compounds promoted by potassium hydroxide have great potentials in industrial applications. On the other hand, naphthopyran derivatives, which have attracted considerable attention due to their interesting photochromic properties and biological applications,[6] are obtained via a Claisen rearrangement of alkynyl aryl ethers from propargylic alcohols and naphthols under acid catalysis in an aprotic solvent (toluene, CH_2Cl_2, $CHCl_3$, CH_3CN) amongst the traditional methods.[2a,7] However, these procedures required a harmful organic solvent as the reaction medium. Therefore, the development of naphthoran preparation in the solid state would overcome such problem. Even though the synthesis of naphthorans catalyzed by *p*-toluenesulfonic acid in the solid state has recently been reported,[8] in which equal amount of *p*-TsOH was used. It will be of great interest if a synthetic route for naphthopyrans by a catalytic amount of Lewis acid can be developed with high yield under solvent-free conditions.

Mechanical inducement via high-energy ball milling is a scalable experimental technique, which is well established for the grinding and modification of inorganic materials.[9] Recently, this technique has been successfully utilized to promote solvent-free mechanochemical reactions and offers the advantages of environmentally benign processes, low costs, simplicity in process and handling, and even higher selectivity.[10] Our research group has reported the application of this technique to solvent-free fullerene[11] and non-fullerene[12] reactions. Herein, we report the solvent-free alkynylations of terminal alkynes with carbonyl compounds to generate propargylic alcohols under ball-milling conditions, and the subsequent cyclizations of propargylic alcohols with 2-naphthol leading to naphthopyrans under the same solvent-free conditions.

2. Results and discussion

In our present investigation, all of the solvent-free reactions were carried out under ball-milling conditions. The nucleophilic addition reactions of terminal alkynes (**1a**–**d**) with carbonyl compounds (**2a**–**l**) were found to proceed efficiently at ambient temperature in short reaction time. In these reactions, one or more

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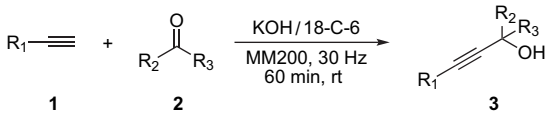
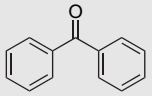
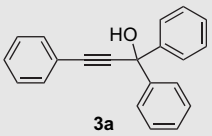
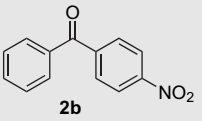
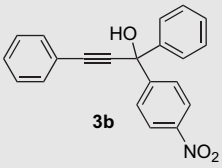
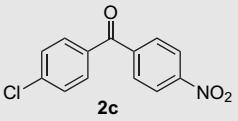
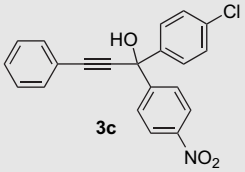
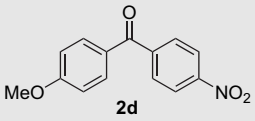
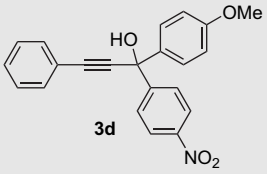
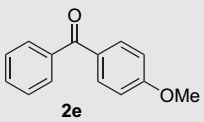
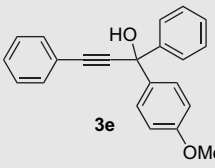
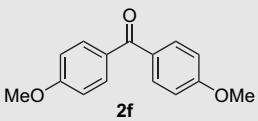
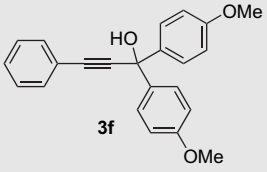
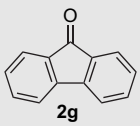
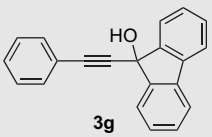
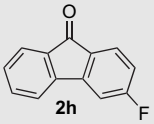
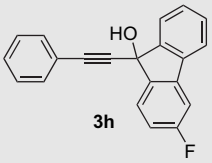
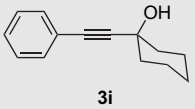
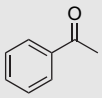
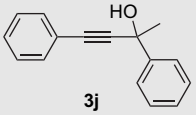
Table 1
Nucleophilic addition reactions of terminal alkynes with carbonyl compounds promoted by KOH in the presence of 18-crown-6[a]

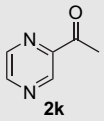
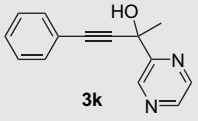
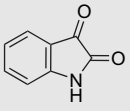
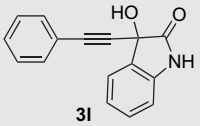
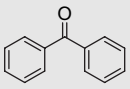
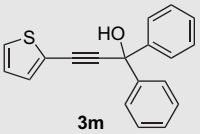
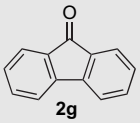
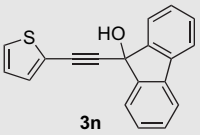
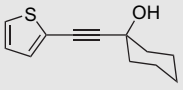
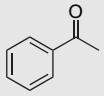
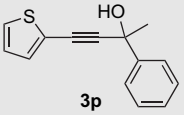
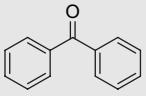
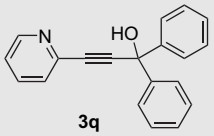
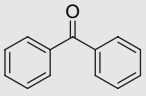
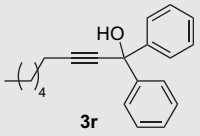


1 2 3

Entry	R_1	2	Product	Yield[b] (%)
1	 **1a**	 **2a**	 **3a**	97
2	 **1a**	 **2b**	 **3b**	95
3	 **1a**	 **2c**	 **3c**	92
4	 **1a**	 **2d**	 **3d**	93
5	 **1a**	 **2e**	 **3e**	81
6[c]	 **1a**	 **2f**	 **3f**	61
7	 **1a**	 **2g**	 **3g**	92
8	 **1a**	 **2h**	 **3h**	90
9	 **1a**	 **2i**	 **3i**	89
10	 **1a**	 **2j**	 **3j**	83

(*continued on next page*)

Table 1 (*continued*)

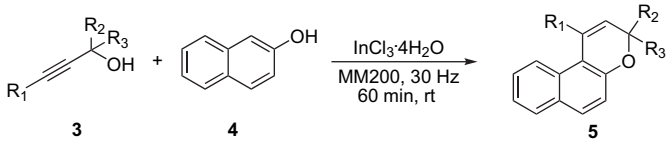
Entry	R_1	2	Product	Yield[b] (%)
11	 **1a**	 **2k**	 **3k**	81
12	 **1a**	 **2l**	 **3l**	91
13	 **1b**	 **2a**	 **3m**	96
14	 **1b**	 **2g**	 **3n**	94
15	 **1b**	 **2i**	 **3o**	91
16	 **1b**	 **2j**	 **3p**	79
17	 **1c**	 **2a**	 **3q**	91
18	 **1d**	 **2a**	 **3r**	54

[a] All reactions were carried out by ball milling at 30 Hz for 1 h.
[b] Isolated yield.
[c] Reaction time was 2 h.

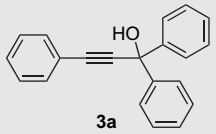
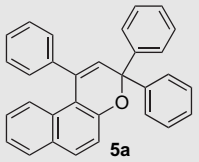
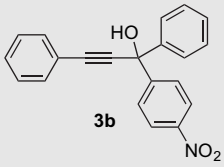
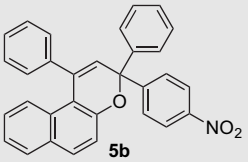
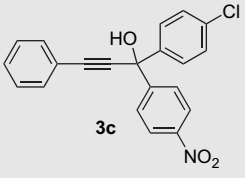
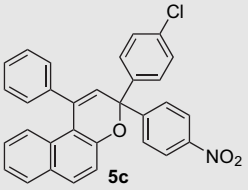
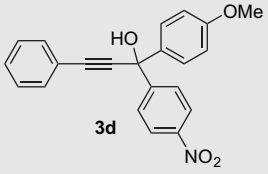
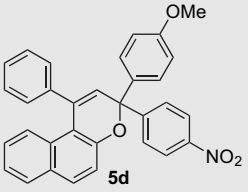
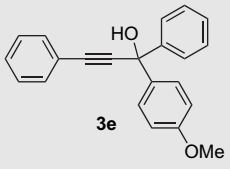
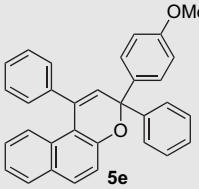
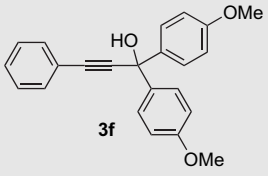
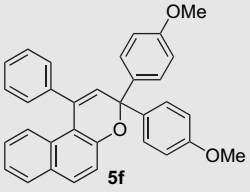
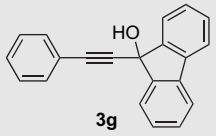
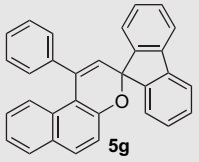
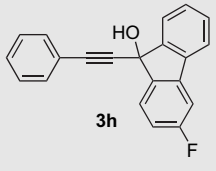
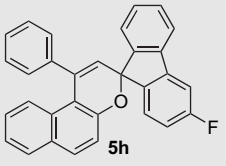
equivalents of KOH were necessary for the nucleophilic addition reactions. The addition of 18-crown-6 would improve the yields significantly in this procedure. The reaction results for the addition reactions of terminal alkynes **1a**–**d** with carbonyl compounds **2a**–**l** promoted by KOH in the presence of 18-crown-6 are listed in Table 1.

From Table 1, it can be seen that the nucleophilic addition reactions of terminal alkynes **1a**–**d** with carbonyl compounds **2a**–**l** generally gave products (**3a**–**r**) in moderate to high yields (54–97%). It's noteworthy that the yields for the reaction of phenylacetylene (**1a**) with diarylketones (**2a**–**f**) bearing different functional groups varied significantly, ranging from 61% to 97%. For the substrate without any substituent on the two aryl groups (**3a**) or substrates bearing an electron-withdrawing group on at least one of the two aryl groups such as **3b**, **3c** and **3d**, the reactions proceeded efficiently, affording the products in 92–97% yields (Table 1, entries 1–4). By introducing an electron-donating group into one or both of the aryl groups of the diarylketones, the product yields were severely decreased (Table 1, entries 5 and 6). For ketone **2f** bearing two electron-donating groups, the reaction was hard to achieve completion, and only a low yield of 61% was obtained even though the reaction time was prolonged to 2 h (Table 1, entry 6). For the reaction of **1a** with cyclic ketones (**2g**–**i**), high yields (89–92%) were obtained (Table 1, entries 7–9). When a methyl ketone was used for this reaction in organic solvent, some amount of byproduct was usually formed due to the competitive aldol condensation, in which the methyl ketone must be added slowly to prevent the side reaction.[13] However, under our solvent-free conditions, good yields could be readily achieved even the reactants were added in one pot for methyl ketones **2j** and **2k** (Table 1, entries 10 and 11). If isatin (**2l**) was used to react with phenylacetylene, 91% yield was achieved (Table 1, entry 12). The reaction could be extended to other heterocyclic alkynes such as 2-thienylacetylene (**1b**) and 2-pyridinylacetylene (**1c**) and aliphatic alkynes such as 1-octyne (**1d**). The

Table 2
Cycloaddition reactions of propargylic alcohols with 2-naphthol catalyzed by indium trichloride tetrahydrate[a]

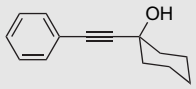
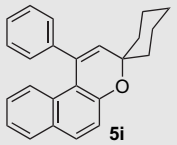
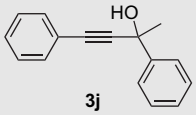
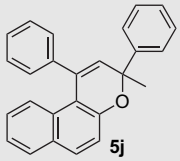
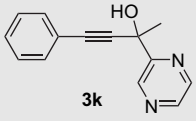
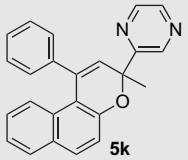
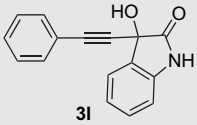
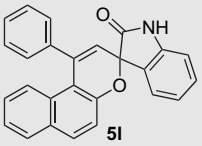
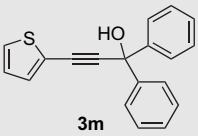
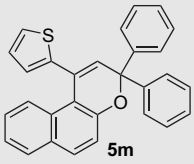
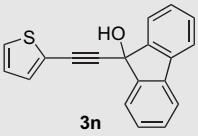
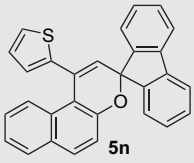
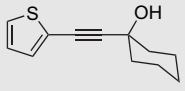
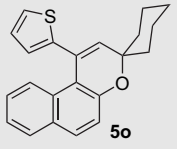
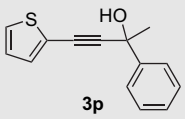
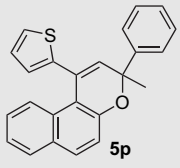
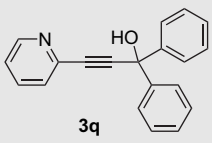
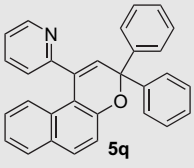
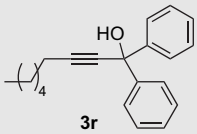
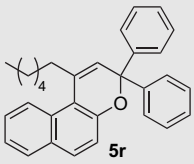


3 4 5

Entry	3	Product	Yield[b] (%)
1			97
2			96
3			95
4			90
5			97
6			93
7			93
8			97

(*continued*)

Table 2 (*continued*)

Entry	3	Product	Yield[b] (%)
9			76
10			92
11			0
12[c]			82
13			93
14			93
15			82
16			95
17			0
18			95

[a] All reactions were carried out by ball milling at 30 Hz for 1 h.
[b] Isolated yield.
[c] The amount of $InCl_3 \cdot 4H_2O$ was 150 mol %.

reaction of **1b** with representative carbonyl compounds proceeded efficiently and afforded good to high yields (79–96%) (Table 1, entries 13–16). The reaction of **1c** with benzophenone (**2a**) also gave the expected product in a high yield (91%) (Table 1, entry 17). However, the reaction of **1d** with **2a** was hard to proceed and only moderate yield (54%) was obtained (Table 1, entry 18).

We've also examined other bases for the nucleophilic addition reaction. When weak inorganic base (K_2CO_3) along with 18-crown-6 or conventional organic base (CH_3ONa, DBU or DABCO) was used, no target product was formed. When a catalytic amount of KOH/18-crown-6 was used, only moderate yield of the desired product could be obtained.

Under the same ball-milling conditions, the synthesized propargylic alcohols **3a**–**r** were further transformed into naphthopyrans (**5a**–**r**) by their cyclization reactions with 2-naphthol (**4**). The reactions of propargylic alcohols **3a**–**r** with **4** except for **3k** and **3q** could proceed well when catalyzed by a Lewis acid. In these reactions, a catalytic amount of $InCl_3\cdot 4H_2O$ showed high efficiency for the cycloaddition reactions. When the reactions were catalyzed by other Lewis acids such as $ZnCl_2$ or $SnCl_4$, the corresponding yields of naphthopyrans were slightly decreased. But the yield for product **5l** decreased dramatically even with excess $ZnCl_2$ or $SnCl_4$. After further screening, 20 mol % of $InCl_3\cdot 4H_2O$ was employed for the cyclization reactions.

The reaction results for the cyclization reactions of propargylic alcohols **3a**–**r** with 1.2 equiv of naphthol **4** catalyzed by 20 mol % $InCl_3\cdot 4H_2O$ were listed in Table 2. From Table 2, it can be seen that the cyclization reactions gave naphthopyran products in 90–97% yields from propargylic alcohols **3a**–**h**, **3j**, **3m**, **3n**, **3p** and **3r** bearing different substituents (Table 2, entries 1–8, 10, 13, 14, 16 and 18). Lower yields (76% and 82%) were obtained from 1-(phenylethynyl)cyclohexanol **3i** and 1-(thiophen-2-ylethynyl)cyclohexanol **3o** (Table 2, entries 9 and 15), the exact reason for this phenomenon is unknown right now. The yield of product **5l** was increased from 23% to 82% by increasing the usage of the catalyst from 0.2 to 1.5 equiv (Table 2, entry 12). Propargylic alcohols **3k** bearing a pyrazinyl group and **3q** bearing a pyridyl group failed to afford the desired naphthopyran product even with excess (1.5 equiv) of $InCl_3\cdot 4H_2O$ (Table 2, entries 11 and 17), probably due to the unwanted coordination of the pyrazinyl or pyridyl ligand to the indium metal.

Compared with the reported methods, the main advantages of the present procedure are milder reaction conditions, higher yields, shorter reaction time and no side reactions. For example, previous method for synthesizing compound **5f** was carried out in toluene at 50 °C for 1.5 h with acidic alumina as a catalyst, and the corresponding yield was as low as 76%.[7d] Whereas under our ball-milling conditions, 93% yield of compound **5f** was achieved at ambient temperature for 1 h. The above reactions had also been tentatively carried out in organic solvents. However, the results were much poorer than those of the current mechanical milling procedure. The reason for the efficiency of the current solvent-free procedure should rely on an enhanced reaction rate resulted from ultimately high concentrations of reactants without using solvent.

3. Conclusion

In summary, we have presented a practical method for the preparation of propargylic alcohols from terminal alkynes and carbonyl compounds promoted by KOH in the presence of 18-crown-6, and subsequent efficient cyclizations of propargylic alcohols with 2-naphthol catalyzed by $InCl_3\cdot 4H_2O$ under the solvent-free ball-milling conditions. These reactions were carried out without the usage of any solvent, and the products were obtained in synthetic valuable yields. Ball-milling exhibits its superiority over the reported methods in the preparation of propargylic alcohols and naphthopyran derivatives. The advantages of this procedure including mild condition, high yield, short reaction time and easy work-up procedure made the present method a convenient, effective and environmentally friendly one, which could serve as an attractive alternative to the traditional methodology.

4. Experimental

4.1. General

Reagents and solvents were obtained from commercial suppliers and were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, at 300 MHz and 75 MHz, respectively, on a 300 MHz spectrometer with chemical shifts (δ) were reported in parts per million relative to tetramethylsilane. Splitting patterns were designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. All intensities in the ^{13}C NMR spectral data are 1C except where indicated. FTIR spectra were taken in KBr pellets and reported in cm^{-1}. High-resolution mass spectra (HRMS) were recorded with an EI mode. Analytical TLC and column chromatography were performed on silica gel GF_{254}, and silica gel H_{60}, respectively.

4.2. Typical procedure for the preparation of propargylic alcohols (3)

A mixture of terminal alkyne **1a** (**1b**–**d**, 0.24 mmol), 18-crown-6 (0.24 mmol), potassium hydroxide (0.2 mmol), carbonyl compound **2a** (**2b**–**l**, 0.2 mmol) and a stainless-steel ball (D=0.7 mm) was placed into a stainless-steel jar (10 mL). The same mixture was introduced into another parallel jar. The two reaction vessels were closed and fixed on the vibration arms of a ball-milling apparatus (Retsch MM200 mixer mill, Retsch GmbH, Haan, Germany) and were milled vigorously at a rate of 1800 rpm at room temperature for 1 h. The resulting mixtures were extracted with ethyl acetate and the desired product was separated by flash column chromatography over silica gel.

4.3. Typical procedure for the preparation of naphthopyrans (5)

A mixture of propargylic alcohols **3a** (**3b**–**r**, 0.2 mmol), naphthol **4** (0.24 mmol) and indium trichloride tetrahydrate (0.04 mmol, 20 mol %) and a stainless-steel ball was placed into a stainless-steel jar. The same mixture was introduced into another parallel jar. The two reaction vessels were closed and fixed on the vibration arms of a ball-milling apparatus. The reactants were milled vigorously at a rate of 1800 rpm at room temperature for 1 h. The resulting mixtures were extracted with ethyl acetate and the desired product was separated by flash column chromatography on silica gel.

Compounds **5a**[14] and **5f**[7d] have been previously reported and their identities were confirmed by comparison with their reported data. Spectroscopic data of the newly synthesized compounds (**5b**–**e**, **5g**–**j**, **5l**–**p** and **5r**) are given below.

*4.3.1. 3-(4-Nitrophenyl)-1,3-diphenyl-3H-benzo[f]chromene (**5b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, J=9.0 Hz, 2H), 7.75 (d, J=9.0 Hz, 2H), 7.73 (d, J=8.7 Hz, 1H), 7.67 (d, J=8.1 Hz, 1H), 7.54–7.50 (m, 2H), 7.38–7.23 (m, 9H), 7.19 (ddd, J=8.6, 6.6, 1.5 Hz, 1H), 7.08 (d, J=8.2 Hz, 1H), 7.01 (ddd, J=8.2, 6.6, 1.2 Hz, 1H), 6.16 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.3, 151.9, 147.3, 143.3, 140.9, 138.5, 131.5, 130.6, 129.8, 128.7 (2C), 128.6, 128.5 (2C), 128.2, 128.11, 128.08 (2C), 128.0 (2C), 127.7, 127.0 (2C), 126.5, 125.5, 123.7, 123.4 (2C), 118.5, 116.8, 81.7; IR (KBr) ν_{max} 3053, 1620, 1592, 1485, 1447, 1368, 1345, 1299,

1236, 1169, 1092, 1002, 943, 861, 818, 743, 697 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{31}H_{21}NO_3$ 455.1521, found 455.1516.

*4.3.2. 3-(4-Chlorophenyl)-3-(4-nitrophenyl)-1-phenyl-3H-benzo[f]chromene (**5c**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J=8.9 Hz, 2H), 7.74 (d, J=8.8 Hz, 1H), 7.72 (d, J=8.9 Hz, 2H), 7.68 (d, J=8.2 Hz, 1H), 7.46 (d, J=8.6 Hz, 2H), 7.38–7.25 (m, 8H), 7.21 (ddd, J=8.1, 6.3, 1.6 Hz, 1H), 7.07 (d, J=8.5 Hz, 1H), 7.02 (ddd, J=8.5, 6.3, 1.2 Hz, 1H), 6.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 151.4, 147.4, 141.8, 140.6, 138.9, 134.2, 131.7, 130.6, 129.8, 128.8 (2C), 128.7 (2C), 128.6, 128.5 (2C), 128.2, 128.0 (2C), 127.9 (2C), 127.0, 126.5, 125.6, 123.8, 123.6 (2C), 118.4, 116.7, 81.3; IR (KBr) ν_{max} 3054, 1621, 1598, 1519, 1491, 1446, 1347, 1235, 1103, 1071, 1005, 964, 852, 815, 753, 699 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{31}H_{20}{}^{35}ClNO_3$ 489.1132, found 489.1135.

*4.3.3. 3-(4-Methoxyphenyl)-3-(4-nitrophenyl)-1-phenyl-3H-benzo[f]chromene (**5d**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, J=8.9 Hz, 2H), 7.73 (d, J=8.9 Hz, 2H), 7.72 (d, J=8.9 Hz, 1H), 7.67 (d, J=8.1 Hz, 1H), 7.41 (d, J=8.9 Hz, 2H), 7.38–7.30 (m, 6H), 7.19 (ddd, J=8.0, 6.6, 1.4 Hz, 1H), 7.07 (d, J=8.5 Hz, 1H), 7.01 (ddd, J=8.5, 6.6, 1.2 Hz, 1H), 6.81 (d, J=8.9 Hz, 2H), 6.12 (s, 1H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 152.29, 152.26, 147.2, 140.9, 138.3, 135.1, 131.4, 130.5, 129.8, 128.7 (2C), 128.6, 128.5 (2C), 128.1 (3C), 127.92 (2C), 127.89, 126.5, 125.5, 123.6, 123.4 (2C), 118.5, 116.7, 113.8 (2C), 81.6, 55.3; IR (KBr) ν_{max} 3055, 2930, 2835, 1622, 1605, 1514, 1346, 1251, 1234, 1175, 1003, 959, 853, 826, 748, 698 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{32}H_{23}NO_4$ 485.1627, found 485.1635.

*4.3.4. 3-(4-Methoxyphenyl)-1,3-diphenyl-3H-benzo[f]-chromene (**5e**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J=8.9 Hz, 1H), 7.66 (d, J=8.2 Hz, 1H), 7.55–7.50 (m, 2H), 7.44 (d, J=8.8 Hz, 2H), 7.34–7.31 (m, 5H), 7.31–7.24 (m, 3H), 7.23–7.13 (m, 2H), 7.08 (d, J=8.6 Hz, 1H), 6.98 (ddd, J=8.6, 6.6, 1.2 Hz, 1H), 6.78 (d, J=8.8 Hz, 2H), 6.16 (s, 1H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 152.7, 144.9, 141.5, 137.2, 136.5, 130.9, 130.4, 129.9, 129.7, 128.7 (2C), 128.6 (2C), 128.5, 128.13 (2C), 128.12 (2C), 127.7, 127.5, 127.1 (2C), 126.6, 125.1, 123.2, 118.9, 116.7, 113.5 (2C), 82.1, 55.3; IR (KBr) ν_{max} 3056, 2930, 2835, 1623, 1607, 1510, 1459, 1444, 1254, 1235, 1175, 1072, 1030, 1002, 953, 832, 813, 748, 701 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{32}H_{24}O_2$ 440.1776, found 440.1779.

*4.3.5. 1-Phenylspiro[benzo[f]chromene-3,9′-fluorene] (**5g**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J=8.2 Hz, 1H), 7.74 (d, J=8.8 Hz, 1H), 7.66 (d, J=7.5 Hz, 2H), 7.44 (d, J=7.5 Hz, 2H), 7.38 (t, J=7.5 Hz, 2H), 7.36–7.09 (m, 11H), 5.92 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.7, 146.6 (2C), 141.4, 139.7 (2C), 138.4, 130.8, 130.7, 130.1 (2C), 129.9, 128.7, 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.8, 126.6, 126.3, 125.4, 125.3 (2C), 123.5, 120.2 (2C), 119.1, 116.6, 84.6; IR (KBr) ν_{max} 3054, 2923, 1622, 1589, 1509, 1490, 1447, 1367, 1344, 1236, 1155, 1120, 1002, 942, 821, 759, 738, 700 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{31}H_{20}O$ 408.1514, found 408.1508.

*4.3.6. 3′-Fluoro-1-phenylspiro[benzo[f]chromene-3,9′-fluorene] (**5h**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J=8.2 Hz, 1H), 7.75 (d, J=8.9 Hz, 1H), 7.62 (d, J=7.6 Hz, 1H), 7.47–7.26 (m, 10H), 7.22–7.15 (m, 3H), 7.12 (ddd, J=8.7, 6.7, 1.3 Hz, 1H), 6.81 (td, J=8.7, 2.4 Hz, 1H), 5.90 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5 (d, ^1J=247.4 Hz), 154.6, 147.3, 142.2 (d, ^3J=11.9 Hz), 142.1, 141.2, 138.6 (d, ^4J=2.8 Hz), 138.5, 130.9, 130.7, 130.2, 129.9, 129.1, 128.8, 128.7 (2C), 128.0 (2C), 127.8, 126.6 (d, ^3J=9.3 Hz), 126.5, 125.8, 125.5, 125.3, 123.6, 120.4, 119.0, 116.5, 115.0 (d, ^2J=22.9 Hz), 107.5 (d, ^2J=23.6 Hz), 84.0; IR (KBr) ν_{max} 3056, 1623, 1596, 1519, 1489, 1345, 1233, 1091, 1005, 962, 853, 818, 750, 698 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{31}H_{19}FO$ 426.1420, found 426.1418.

*4.3.7. 1-Phenylspiro[benzo[f]chromene-3,1′-cyclohexane] (**5i**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.75–7.70 (m, 2H), 7.34–7.29 (m, 3H), 7.23–7.17 (m, 4H), 7.09 (d, J=8.5 Hz, 1H), 7.02 (ddd, J=8.5, 6.6, 1.2 Hz, 1H), 5.73 (s, 1H), 1.96–1.92 (m, 2H), 1.82–1.67 (m, 4H), 1.58–1.43 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.9, 141.9, 135.8, 130.4, 130.3, 130.12, 130.08, 128.5 (3C), 128.0 (2C), 127.4, 126.5, 125.1, 123.0, 118.9, 116.9, 76.4, 34.7 (2C), 25.7, 22.0 (2C); IR (KBr) ν_{max} 3054, 2931, 2853, 1622, 1593, 1511, 1444, 1369, 1343, 1232, 1072, 987, 816, 752, 701 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{24}H_{22}O$ 326.1671, found 326.1668.

*4.3.8. 3-Methyl-1,3-diphenyl-3H-benzo[f]chromene (**5j**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J=9.1 Hz, 1H), 7.66 (d, J=8.1 Hz, 1H), 7.60–7.56 (m, 2H), 7.36–7.21 (m, 8H), 7.18–7.12 (m, 2H), 7.03 (d, J=8.6 Hz, 1H), 6.97 (ddd, J=8.6, 6.5, 1.2 Hz, 1H), 6.07 (s, 1H), 1.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 145.5, 141.6, 136.9, 130.7, 130.3, 130.0, 129.6, 128.6 (2C), 128.5, 128.12 (2C), 128.07 (2C), 127.6, 127.4, 126.6, 125.6 (2C), 125.1, 123.2, 118.8, 116.6, 78.3, 29.9; IR (KBr) ν_{max} 3055, 2928, 1625, 1592, 1512, 1490, 1445, 1370, 1343, 1236, 1101, 1073, 980, 894, 824, 769, 748, 737, 698 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{26}H_{20}O$ 348.1514, found 348.1510.

*4.3.9. 1-Phenylspiro[benzo[f]chromene-3,3′-indolin]-2′-one (**5l**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.90 (d, J=8.0 Hz, 1H), 7.78 (d, J=8.3 Hz, 1H), 7.74–7.65 (m, 3H), 7.58–7.48 (m, 4H), 7.40 (ddd, J=8.0, 6.9, 1.1 Hz, 1H), 7.31 (ddd, J=8.2, 6.9, 1.3 Hz, 1H), 7.23 (t, J=7.7 Hz, 1H), 7.08 (d, J=7.5 Hz, 1H), 6.98 (td, J=7.5, 0.8 Hz, 1H), 6.90 (d, J=7.7 Hz, 1H), 4.88 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5, 152.2, 147.7, 141.7, 132.9, 131.0, 130.9, 130.6, 129.1, 129.0, 128.9, 128.8, 128.4, 128.2, 127.6, 126.2, 126.0, 124.8, 124.5, 123.6, 123.3, 122.8, 122.0, 112.5, 110.4, 45.7; IR (KBr) ν_{max} 3179, 3145, 3066, 2906, 1699, 1617, 1471, 1393, 1326, 1214, 1004, 981, 812, 752, 703 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{26}H_{17}NO_2$ 375.1259, found 375.1261.

*4.3.10. 3,3-Diphenyl-1-(thiophen-2-yl)-3H-benzo[f]chromene (**5m**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J=8.9 Hz, 1H), 7.67 (d, J=8.2 Hz, 1H), 7.55–7.50 (m, 4H), 7.34–7.17 (m, 10H), 7.10 (ddd, J=8.7, 6.7, 1.3 Hz, 1H), 7.01 (dd, J=5.1, 3.6 Hz, 1H), 6.93 (dd, J=3.6, 1.1 Hz, 1H), 6.32 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 144.4 (2C), 143.0, 131.3, 130.7, 130.5, 130.0, 129.9, 128.5, 128.2 (4C), 127.7 (2C), 127.4, 127.3 (4C), 126.6, 126.3, 125.3, 125.1, 123.5, 118.8, 116.8, 82.4; IR (KBr) ν_{max} 3057, 2925, 1619, 1602, 1509, 1491, 1445, 1350, 1232, 1219, 1205, 999, 956, 811, 755, 703 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{29}H_{20}OS$ 416.1235, found 416.1236.

*4.3.11. 1-(Thiophen-2-yl)spiro[benzo[f]chromene-3,9′-fluorene] (**5n**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J=7.8 Hz, 1H), 7.76 (d, J=8.7 Hz, 1H), 7.67 (d, J=7.5 Hz, 2H), 7.50–7.13 (m, 11H), 7.02 (dd, J=5.1, 3.6 Hz, 1H), 6.92 (dd, J=3.6, 1.1 Hz, 1H), 6.07 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 146.3 (2C), 143.0, 139.8 (2C), 131.8, 131.1, 130.8, 130.1 (2C), 129.9, 128.7, 128.5 (2C), 127.4, 126.9, 126.5, 126.2, 125.5, 125.3 (2C), 125.2, 123.7, 120.2 (2C), 119.0, 116.6, 84.5; IR (KBr) ν_{max} 3058, 2926, 1618, 1587, 1508, 1449, 1367, 1299, 1259, 1233, 1119, 1001, 819, 757, 738, 703 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{29}H_{18}OS$ 414.1078, found 414.1071.

*4.3.12. 1-(Thiophen-2-yl)spiro[benzo[f]chromene-3,1′-cyclohexane] (**5o**)*

^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J=8.4 Hz, 2H), 7.32 (d, J=8.7 Hz, 1H), 7.27–7.20 (m, 3H), 7.13 (ddd, J=8.4, 6.2, 1.2 Hz, 1H), 6.98 (dd, J=5.1, 3.6 Hz, 1H), 6.81 (dd, J=3.6, 1.1 Hz, 1H), 5.88 (s, 1H), 1.99–1.91 (m, 2H), 1.81–1.64 (m, 4H), 1.58–1.40 (m, 4H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 152.7, 143.6, 130.7 (2C), 130.3, 130.0, 129.1, 128.5, 127.2, 126.1 (2C), 125.1, 124.6, 123.2, 118.8, 116.8, 76.3, 34.5 (2C), 25.6, 21.9 (2C); IR (KBr) ν_{max} 2934, 2857, 1622, 1511, 1457, 1447, 1434, 1371, 1234, 1031, 988, 814, 751, 698 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{22}H_{20}OS$ 332.1235, found 332.1234.

4.3.13. 3-Methyl-3-phenyl-1-(thiophen-2-yl)-3H-benzo[f]chromene (**5p**)

^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J=8.8 Hz, 1H), 7.68 (d, J=8.1 Hz, 1H), 7.58–7.53 (m, 2H), 7.31–7.14 (m, 7H), 7.08 (t, J=7.7 Hz, 1H), 7.01 (dd, J=5.1, 3.6 Hz, 1H), 6.88 (dd, J=3.6, 1.1 Hz, 1H), 6.22 (s, 1H), 1.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 145.2, 143.2, 131.1, 130.4, 130.3, 130.1, 129.9, 128.5, 128.2 (2C), 127.5, 127.3, 126.4, 126.3, 125.6 (2C), 125.2, 125.0, 123.4, 118.7, 116.6, 78.3, 29.6; IR (KBr) ν_{max} 3059, 2985, 1620, 1592, 1512, 1444, 1369, 1345, 1234, 1178, 1096, 1074, 979, 894, 820, 763, 744, 698 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{24}H_{18}OS$ 354.1078, found 354.1085.

4.3.14. 1-Hexyl-3,3-diphenyl-3H-benzo[f]chromene (**5r**)

^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J=8.6 Hz, 1H), 7.69 (d, J=8.0 Hz, 1H), 7.62 (d, J=8.8 Hz, 1H), 7.48–7.43 (m, 4H), 7.39 (ddd, J=8.1, 6.9, 1.2 Hz, 1H), 7.30–7.18 (m, 8H), 6.03 (s, 1H), 2.91 (t, J=7.6 Hz, 2H), 1.59–1.47 (m, 2H), 1.38–1.19 (m, 6H), 0.83 (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 145.1 (2C), 136.4, 130.6, 130.3 (2C), 129.0, 128.0 (4C), 127.4 (2C), 127.3 (4C), 127.2, 126.0, 125.1, 123.2, 119.0, 118.2, 82.2, 35.6, 31.6, 29.3, 29.1, 22.7, 14.1; IR (KBr) ν_{max} 2954, 2928, 1628, 1595, 1514, 1492, 1471, 1448, 1369, 1226, 1006, 960, 810, 752, 698 cm^{-1}; HRMS (EI^+, m/z [M^+]) calcd for $C_{31}H_{30}O$ 418.2297, found 418.2302.

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