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Versatile synthesis of (*Z*)-1-alkylidene-1,3-dihydroisobenzofurans and 1*H*-isochromenes by palladium-catalyzed cycloisomerization of 2-alkynylbenzyl alcohols

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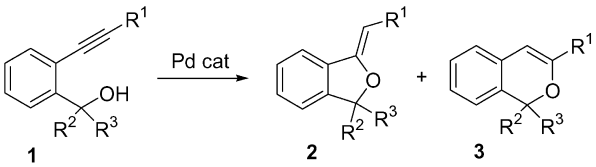
Abstract—An easy synthesis of (*Z*)-1-alkylidene-1,3-dihydroisobenzofurans and 1*H*-isochromenes by palladium-catalyzed cycloisomerization of readily available 2-alkynylbenzyl alcohols under neutral conditions is reported. Reactions were carried out at 70–100°C in the presence of catalytic amounts (1–2%) of PdI_2 in conjunction with 2 equiv. of KI for 1.5–24 h. The preference towards the 5-*exo-dig* cyclization mode (leading to 1,3-dihydroisobenzofurans) or the 6-*endo-dig* cyclization mode (leading to isochromenes) turned out to be dependent on the substitution pattern of the substrate as well as reaction conditions. In several cases, by properly adjusting the reaction conditions, the same substrate could be selectively converted into either the dihydroisobenzofuran or the 1*H*-isochromene derivative.

1. Introduction

Palladium catalysis has recently acquired an increasing importance in the synthesis of heterocycles.[1] Methods based on annulation of acyclic substrates bearing suitably placed nucleophilic and electrophilic functions are particularly attractive, since they can regioselectively afford the heterocyclic ring with the desired substitution pattern under essentially neutral conditions. We have already described several approaches to the Pd(II)-catalyzed synthesis of heterocyclic derivatives starting from acetylenic substrates, by a simple cycloisomerization approach[2] as well as by carbonylative cyclization reactions.[3]

We now wish to report an extension of our Pd(II)-catalyzed cycloisomerization methodology to readily available 2-alkynylbenzyl alcohols **1** for the synthesis of (*Z*)-1-alkylidene-1,3-dihydroisobenzofurans and 1*H*-isochromenes (**2** and **3**, respectively, Eq. (1)) under neutral conditions.



(1)

Cycloisomerization of **1** to **2** and **3** has been previously reported to occur under basic conditions, with NaOH,[4] NaH[4] or TBAF[5] as the base. These reactions occurred with satisfactory yields only when R^1 was an aryl group, leading to **2** or **3** depending on the substitution pattern on R^1,[4] while with R^1=alkyl the final product **3** was obtained with yields not higher than 10%.[5] The PdI_4^{2-}-catalyzed methodology reported in this work can be successfully applied to substrates bearing R^1=alkyl or aryl. Moreover, it has been found that not only the substitution pattern of the substrate, but also reaction conditions can direct the catalytic process towards the anti 5-*exo-dig* cyclization mode leading to **2** or the 6-*endo-dig* cyclization mode leading to **3** (Scheme 1; anionic iodide ligands are omitted for clarity).[6]

2. Results and discussion

We started our investigation with 2-ethynylbenzyl alcohol **1a**, readily available from (2-iodophenyl)methanol through Pd/Cu-catalyzed coupling with ethynyltrimethylsilane to give [2-(trimethylsilanyl)ethynylphenyl]methanol **1a′** followed by deprotection. The reaction of **1a** carried out under

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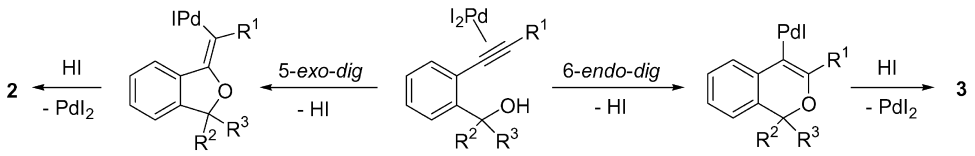
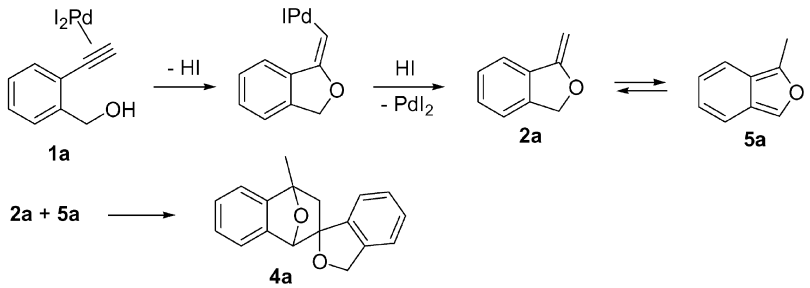


Scheme 1.

Table 1. Reactions of 2-(ethynylphenyl)methanol **1a** in different solvents in the presence of PdI_2 (0.01 equiv.) and KI (0.02 equiv.)

Entry	Solvent	Convn of **1a** (%)[a]	Yield of **4a** (%)[b]
1[c]	DMA	100	Traces
2	DME	100	14
3	Dioxane	100	6
4	MeOH	98	4
5	MeCN	100	17
6[d]	MeCN	82	9
7[e]	MeCN	95	10
8[f]	MeCN	100	Traces
9[g]	MeCN	100	Traces

Unless otherwise noted, all reactions were carried out under nitrogen using anhydrous solvents (2 mmol of **1a**/mL of solvent, 3–5 mmol scale based on **1a**) at 80°C for 2 h.
[a] Determined via GLC.
[b] Based on starting **1a**, by GLC.
[c] Reaction time was 3 h.
[d] Substrate concentration was 0.5 mmol/mL MeCN.
[e] Reaction temperature was 70°C.
[f] The reaction was carried out with $PdCl_2$ (0.01 equiv.) and KCl (0.02 equiv.).
[g] The reaction was carried out with $(PhCN)_2PdCl_2$ (0.01 equiv.).



Scheme 2.

conditions similar to those previously employed for the synthesis of furans from (*Z*)-2-en-4-yn-1-ols[2c,d] [PdI_2+2 equiv. of KI as the catalyst with **1a**/PdI_2 molar ratio of 100 at 80°C in *N*,*N*-dimethylacetamide (DMA) as the solvent, substrate conc.=2 mmol/mL of DMA] led after 3 h to the formation of traces of a spiro derivative **4a** together with unidentified heavy products at total substrate conversion (entry 1, Table 1).

Formation of **4a** can be easily interpreted as occurring through palladium-mediated 5-*exo-dig* cycloisomerization to give the corresponding 1-methylene-1,3-dihydroisobenzofuran **2a** in equilibrium with its isobenzofuran tautomer **5a**, followed by Diels–Alder cycloaddition between **2a** and **5a** (Scheme 2, anionic iodide ligands are omitted for clarity).

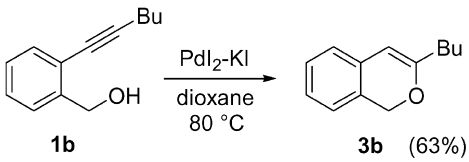
In the attempt of minimizing substrate oligo- and/or polymerization reactions, the reaction was also conducted in different solvents, such as 1,2-dimethoxyethane (DME), 1,4-dioxane, MeOH and MeCN (Table 1, entries 2–5). Low yields of **4a** were consistently obtained, the highest value (17%) being observed in MeCN (entry 5). The yield could not be improved even by decreasing substrate concentration (entry 6) and reaction temperature (entry 7), or by changing the counterion from iodide to chloride (entries 8 and 9).

A markedly different behavior was observed with substrates bearing an internal rather than a terminal triple bond. Thus, the reaction of (2-hex-1-ynylphenyl)methanol **1b** carried out in DMA at 80°C for 2.5 h (substrate conc.=2 mmol/mL of DMA) in the presence of PdI_2 (0.02 equiv.) and KI (0.04 equiv.) afforded 3-butyl-1*H*-isochromene **3b** in 20% yield through a 6-*endo-dig* process (Scheme 1) at 85% substrate conversion (Table 2, entry 1). The reaction was then carried out in different solvents (entries 2–5); the best results both in terms of yield and substrate conversion rate were obtained in dioxane (entry 5). By using dioxane and prolonging the reaction time to 3 h, substrate conversion reached 100% and product GLC yield 70% (63% isolated, entry 6 and Eq. (2)).

Table 2. Synthesis of 3-butyl-1*H*-isochromene **3b** by PdI_2/KI-catalyzed cycloisomerization of (2-hex-1-ynylphenyl)methanol **1b**

Entry	Solvent	Convn of **1b** (%)[a]	Yield of **3b** (%)[b]
1	DMA	85	20
2	DME	77	26
3	MeCN	94	30
4	MeOH	886	58
5	Dioxane	96	69
6[c]	Dioxane	100	70 (63)

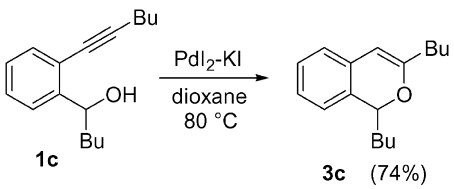
Unless otherwise noted, all reactions were carried out under nitrogen using anhydrous solvents (2 mmol of **1b**/mL of solvent, 3–5 mmol scale based on **1b**) at 80°C for 2.5 h in the presence of PdI_2 (0.02 equiv.) and KI (0.04 equiv.).
[a] Determined via GLC.
[b] GLC yield (isolated yield) based on **1b**.
[c] Reaction time was 3 h.



(2)

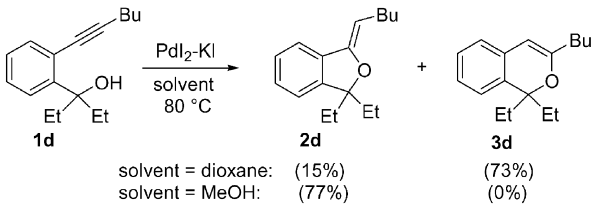
Only very low amounts of **3b** (2–10%) were obtained using $PdCl_2$+2KCl, $(PhCN)_2PdCl_2$, $Pd(OAc)_2$, or $Pd(acac)_2$ as the catalysts under the same conditions. Thus the nature of the Pd(II) counterion plays a fundamental role for the success of the reaction. The reason iodide works much better than chloride or acetate can be related to the greater ability of I^- to act as leaving group with respect to Cl^- or AcO^- in the intramolecular nucleophilic attack step as well as to the higher acidity of HI compared with HCl or AcOH, which favors protonolysis of vinylpalladium intermediate to give the final product (Scheme 1).

1-Alkynylbenzyl alcohols with the triple bond substituted with an alkyl group and bearing a secondary or a tertiary alcoholic group turned out to be more reactive than those bearing a primary alcoholic group. Thus, the reaction of 1-(2-hex-1-ynylphenyl)pentan-1-ol **1c**, carried out in dioxane at 80°C with a substrate/KI/PdI_2 molar ratio of 100/2/1 (substrate conc.=2 mmol/mL of dioxane) required 2 h to achieve complete substrate conversion, affording 1,3-dibutyl-1*H*-isochromene **3c** in 84% GLC yield (74% isolated, Eq. (3)). This result should be compared with that reported in entry 6 (Table 2) for **1b**.



(3)

The higher reactivity for **1c** with respect to **1b** can be ascribed to the steric assistance exerted by the alkyl group α to the –OH, which tends to favor a conformation in which the hydroxyl is closer to the triple bond (reactive rotamer effect).[7] This effect was even more important in the case of 3-(2-hex-1-ynylphenyl)pentan-3-ol **1d**, bearing geminal substitution α to the –OH group. The reaction of this substrate under the same conditions employed for **1c** led after 1.5 h to a mixture of (*Z*)-1,1-diethyl-3-pentylidene-1,3-dihydroisobenzofuran **2d** and 3-butyl-1,1-diethyl-1*H*-isochromene **3d** in 35 and 49% yield, respectively, at total substrate conversion (entry 1, Table 3). Clearly, *gem*-dialkyl substitution causes the –OH group to be still closer to the triple bond, allowing the 5-*exo-dig* mechanism to compete with the 6-*endo-dig* mechanism. Interestingly, working in more dilute conditions resulted in higher selectivity towards **3d**, even though reaction rate was decreased (entries 2 and 3). With 0.1 mmol of **1d** per mL of dioxane, GLC yields of **3d** and **2d** were 78 and 19%, respectively (73 and 15% isolated, entry 3 and Eq. (4)). On the other hand, a completely selective reaction towards **2d** was observed in strongly polar solvents such as DMA or MeOH (entries 4 and 5). By working in MeOH for 2 h, **2d** was obtained in 85% GLC yield (77% isolated, entry 5 and Eq. (4)).



(4)

Substrates **1e–g** with the triple bond substituted with a phenyl group were generally less reactive than the corresponding 2-alkynylbenzyl alcohols **1b–d** with the triple bond substituted with an alkyl group. This is in contrast to what we previously observed for PdI_2/KI-catalyzed cycloisomerization of (*Z*)-en-4-yn-1-ols and (*Z*)-2-en-4-yne-1-thiols, where aryl conjugation to the triple bond led to an increase of reactivity.[2b–d] It is conceivable that extensive conjugation of the triple bond in **1e–g** lowers their coordination ability to Pd(II) thus leading to a decrease of reactivity. Moreover, **1e–g** showed a higher tendency with respect to **1b–d** to undergo 5-*exo-dig* cyclization. This result is in agreement to what previously observed by other Authors for the reaction carried out under basic conditions,[4,5] and can be due to a combination of electronic and stereoelectronic effects exerted by the phenyl group on the triple bond. The reaction of (2-phenylethynylphenyl)methanol **1e** under the same conditions reported in entry 6 (Table 2) for **1b**, but at 90°C rather than 80°C, led to a 52% yield of a 1:1 mixture of (*Z*)-1-benzylidene-1,3-dihydroisobenzofuran **2e** and 3-phenyl-1*H*-isochromene **3e** at 80% substrate conversion (Table 4, entry 1). As for **1d**, selectivity towards the isochromene derivative could be improved by working in more dilute solution: with 0.5 rather than 2 mmol of **1e** per mL of dioxane, after 24 h GLC yields of **2e** and **3e** were 19% (15% isolated) and 45% (40% isolated), respectively, at 90% substrate conversion (entry 2 and Eq. (5)). The reaction was also tested under the same conditions in other solvents, in order to verify also the

Table 3. PdI_2/KI-catalyzed cycloisomerization reactions of 3-(2-hex-1-ynylphenyl)pentan-3-ol **1d** in different solvents

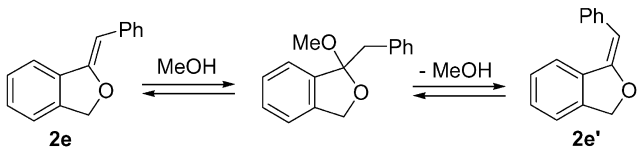
Entry	Solvent	Substrate concn.[a]	*t* (h)	Convn of **1d** (%)[b]	Yield of **2d** (%)[c]	Yield of **3d** (%)[c]
1	Dioxane	2	1.5	100	35	49
2	Dioxane	0.5	4	88	22	61
3	Dioxane	0.1	8	100	19 (15)	78 (73)
4	DMA	2	1.5	100	47	Traces
5	MeOH	2	2	100	85 (77)	0

All reactions were carried out under nitrogen using anhydrous solvents (3–5 mmol scale based on **1d**) at 80°C in the presence of PdI_2 (0.01 equiv.) and KI (0.02 equiv.).
[a] mmol of **1d**/mL of solvent.
[b] Determined via GLC.
[c] GLC yield (isolated yield) based on **1d**.

Table 4. Reactions of 2-(phenylethynylphenyl)methanol **1e** in different solvents in the presence of PdI_2 (0.01 equiv.) and KI (0.02 equiv.)

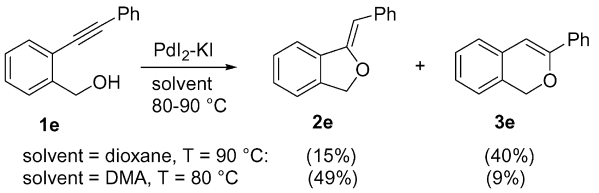
Entry	Solvent	T (°C)	t (h)	Convn of **1e** (%)[a]	Yield of **2e** (%)[b]	Yield of **3e** (%)[b]
1	Dioxane	90	3	80	26	26
2[c]	Dioxane	90	24	90	19 (15)	45 (40)
3	MeCN	90	3	41	12	8
4	MeOH	90	3	100	36[d]	23
5	DMA	90	3	62	30	13
6	DMA	80	3	57	32	8
7[e]	DMA	80	10	95	55 (49)	13 (9)

Unless otherwise noted, all reactions were carried out under nitrogen using anhydrous solvents (2 mmol of **1e**/mL of solvent, 3–5 mmol scale based on **1e**).
[a] Determined via GLC.
[b] GLC yield (isolated yield) based on **1e**.
[c] Substrate concentration was 0.5 mmol/mL of dioxane.
[d] (*E*)-1-Benzylidene-1,3-dihydroisobenzofuran **2e′** was also formed in 10% yield.
[e] The reaction was carried out with 0.02 equiv. of PdI_2 and 0.04 equiv. of KI.



Scheme 3.

50 at 80°C for 10 h, **2e** and **3e** were obtained in 55 and 13% GLC yields (49 and 9% isolated) at 95% substrate conversion (entry 7 and Eq. (5)).



(5)

As expected, secondary and tertiary 2-phenylethynylbenzyl alcohols were more reactive than **1e** and showed a higher tendency towards the 5-*exo-dig* cyclization mode. The results obtained with 1-(2-phenylethynylphenyl)pentan-1-ol **1f** are shown in Table 5. Under the same conditions reported in entry 2 (Table 4) for **1e**, a mixture of 1-benzylidene-3-butyl-1,3-dihydroisobenzofuran **2f** (36% GLC yield) and 1-butyl-3-phenyl-1*H*-isochromene **3f** (30% GLC yield) was obtained at 78% substrate conversion (entry 1, Table 5). Carrying out the reaction at 100°C rather than 90°C, product distribution changed in favor of **3f** (GLC yields for **2f** and **3f** after 4 h were 39 and 43%, respectively, at total substrate conversion, entry 2). As usual, a higher selectivity for **3f** (48% GLC yield, 40% isolated, for **3f** and 30% GLC yield, 27% isolated, for **2f**) was obtained working in more dilute solution (substrate concentration=0.1 rather than 2 mmol per mL of dioxane for 15 h, entry 3 and Eq. (6)). On the

Table 5. Reactions of 1-(2-phenylethynylphenyl)pentan-1-ol **1f** in different solvents in the presence of PdI_2 (0.01 equiv.) and KI (0.02 equiv.)

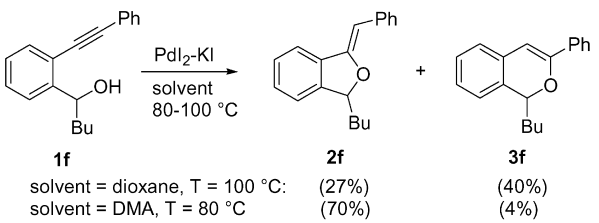
Entry	Solvent	T (°C)	Substrate concn.[a]	t (h)	Convn of **1f** (%)[b]	Yield of **2f** (%)[c]	Yield of **3f** (%)[c]
1	Dioxane	90	0.5	3	78	36	30
2[c]	Dioxane	100	0.5	4	100	39	43
3	Dioxane	100	0.1	15	100	30 (27)	48 (40)
4	DMA	80	2	6	100	76 (70)	6 (4)

All reactions were carried out under nitrogen using anhydrous solvents (3–5 mmol scale based on **1f**).
[a] mmol of **1f**/mL of solvent.
[b] Determined via GLC.
[c] GLC yield (isolated yield) based on **1f**.

possibility to shift the selectivity of the process towards the formation of **2e**. The results obtained in CH_3CN, MeOH and DMA are shown in entries 3–5. Indeed, in all these solvents, **2e** turned out to be the main reaction product. The reaction in CH_3CN (entry 3) was somewhat slower than in MeOH (entry 4) or DMA (entry 5). On the other hand, although MeOH ensured a faster substrate conversion rate compared with DMA, a mixture of stereoisomeric isobenzofurans **2e** and **2e′** was obtained in this solvent,† probably due to reversible MeOH addition to the vinylethereal double bond (Scheme 3). DMA was therefore the solvent of choice for the subsequent experiments (entries 6 and 7), aimed at achieving a good selectivity towards **2e** with complete substrate conversion. Working in this solvent at 80°C rather than 90°C caused a slight decrement of reaction rate and a significant enhancement of the **2e/3e** ratio (from 2.3—entry 5, to 4.0—entry 6) With a substrate to catalyst molar ratio of

† The *E* isomer **2e′** could not be isolated at the pure state from the reaction mixture; however, the same hydrogenated product was obtained from both **2e** and **2e′** by catalytic hydrogenation of the reaction mixture, as shown by GC–MS analysis, thus indicating geometric isomerism.

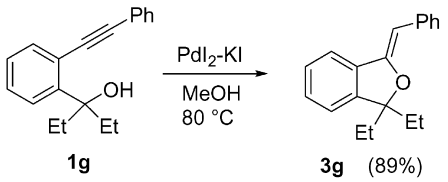
other hand, a selective reaction towards **2f** was attained by using DMA as solvent at 80°C for 6 h with 2 mmol of **1f** per mL of DMA: under these conditions, **2f** was obtained in 76% GLC yield (70% isolated), **3f** being also formed in only 6% GLC yield (4% isolated) at total substrate conversion (entry 4 and Eq. (6)).



(6)

In the case of 3-(2-phenylethynylphenyl)pentan-3-ol **1g** (R^1=Ph, R^2=R^3=Et) bearing geminal substitution α to the hydroxyl group, 5-*exo-dig* cyclization mode leading to 3-benzylidene-1,1-diethyl-1,3-dihydroisobenzofuran **2g** turned out to be the predominant pathway even working in dioxane under dilute conditions. The best results in terms of substrate conversion rate and product yields were

obtained in MeOH under the same conditions reported in entry 5 (Table 3) for **1d**: after 2 h, GLC yield of **2g** was as high as 95% (89% isolated, Eq. (7)) at total substrate conversion.



1g **3g** (89%) (7)

3. Conclusion

In conclusion, we have shown that cycloisomerization of 2-alkynylbenzyl alcohols **1** to (*Z*)-1-alkylidene-1,3-dihydroisobenzofurans **2** (through a 5-*exo-dig* mechanism) and/or 1*H*-isochromenes **3** (through a 6-*endo-dig* mechanism) can be easily achieved under essentially neutral conditions by means of a very simple catalytic system based on PdI_4^{2-} anion. The selectivity of the process proved to be dependent on the substitution pattern of the substrate and reaction conditions, and in several cases it has been possible for the same substrate to direct the process towards the selective formation of either **2** or **3**. In particular, on the basis of the experimental results, the following generalizations can be made: the 5-*exo-dig* cyclization mode tends to be favored by (a) aryl rather than alkyl substitution on the triple bond; (b) alkyl, and especially dialkyl substitution α to the hydroxyl group; (c) a higher solvent polarity; (d) a higher substrate concentration and (e) a lower reaction temperature. On the other hand, the 6-*endo-dig* cyclization mode tends to be favored by (a) alkyl rather than aryl substitution on the triple bond; (b) a lower solvent polarity; (c) more dilute conditions and (d) a higher reaction temperature.

Dihydroisobenzofurans and isochromenes are interesting heterocyclic compounds. Dihydroisobenzofuran are useful precursors of important heterocyclic derivatives,[8] including isobenzofurans[9] and have also found application as synthetic intermediates for the synthesis of biologically active compounds.[10] On the other hand, some isochromene derivatives have showed interesting pharmacological activity;[11] moreover, isochromenes have found application as synthetic intermediates[12] and are potential precursors of isochromanes, whose biological activity is well-known.[13] The reaction reported in this work allows an easy construction of both dihydroisobenzofuran and isochromene rings starting from readily available substrates under mild conditions.

4. Experimental

4.1. General

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, with Me_4Si as internal standard. Chemical shifts and coupling constants (*J*) are given in ppm (δ) and in Hz, respectively. IR spectra were taken on a FT-IR spectrometer. Mass spectra were obtained at 70 eV on a GC–MS apparatus. Microanalyses were performed at our analytical laboratory. Unless otherwise noted, all reactions were carried out under nitrogen using anhydrous solvents and were monitored by TLC on silica gel 60 F_{254} or by GLC using capillary columns with polymethylsilicone+5% phenylsilicone as the stationary phase. Column chromatography was performed on silica gel 60 (70–230 mesh) or neutral alumina 90 (70–230 mesh).

Starting 2-alkynylbenzyl alcohols **1** and their precursors were prepared as described below. All other materials were commercially available and were used without further purification.

4.2. Synthesis of 2-alkynylbenzyl alcohols

2-Alkynylbenzyl alcohols bearing a primary alcoholic group were prepared by Pd/Cu-catalyzed coupling between (2-iodophenyl)methanol and the appropriate alk-1-yne. Substrate **1a** with terminal triple bond was obtained by deprotection of the triple bond of (2-trimethylsilanylethynylphenyl)methanol **1a′** with KF/MeOH. Coupling between an alk-1-yne and 2-bromobenzaldehyde followed by addition of BuLi allowed a facile preparation of substrates bearing a secondary alcoholic group. Substrates bearing a tertiary alcoholic group were easily prepared by coupling between an alk-1-yne and methyl 2-iodobenzoate followed by Grignard reaction.

4.3. Coupling between (2-iodophenyl)methanol and alk-1-ynes

To a stirred solution of (2-iodophenyl)methanol (10.0 g, 42.7 mmol) in anhydrous Et_3N (420 mL) were added $Pd(PPh_3)_4$ [2.0 g (1.73 mmol, R^1=$SiMe_3$) or 4.0 g (3.46 mmol, R^1=Bu, Ph)], CuI [650 mg (3.41 mmol, R^1=$SiMe_3$) or 1.3 g (6.83 mmol, R^1=Bu, Ph)], and $R^1C{\equiv}CH$ (52.0 mmol). The mixture was stirred for 1 h at rt (R^1=$SiMe_3$, Ph) or 60°C (R^1=Bu), and then a saturated solution of NH_4Cl was added at rt followed by CH_2Cl_2. Phases were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4. After removal of the solvent by rotary evaporation, the crude product was purified by column chromatography on silica gel (**1a′**, CH_2Cl_2: pale yellow oil, 8.20 g, 94%; **1b**, 98:2 hexane/AcOEt: pale yellow oil, 6.4 g, 80%; **1e**, 7:3 hexane/AcOEt: pale yellow solid, 6.3 g, 71%) followed in the case of **1e** by repeated crystallization from hexane.

4.4. Deprotection of 1a′ with KF/MeOH

To a stirred solution of **1a′** (5.56 g, 27.2 mmol) in MeOH (143 mL) was added KF (5.65 g, 97.2 mmol). The mixture was allowed to stir at rt for 3 h, and then it was diluted with CH_2Cl_2 and quenched with water. Phases were separated, the aqueous layer extracted with CH_2Cl_2 and the combined organic layers dried over Na_2SO_4. After removal of the solvent by rotary evaporation, the crude product was purified by column chromatography on silica gel (6:4 hexane/AcOEt) followed by repeated crystallization from hexane to give (2-ethynylphenyl)methanol **1a** as a colorless solid (2.6 g, 72%).

4.5. Coupling between 2-bromobenzaldehyde and alk-1-ynes followed by addition of BuLi

The method of Padwa[4] and Dopico[14] was employed. To a stirred solution of 2-bromobenzaldehyde (10.0 g, 54.0 mmol) in anhydrous Et_3N (164 mL) were added $Pd(OAc)_2$ (108 mg, 0.48 mmol), PPh_3 (218 mg, 0.83 mmol), CuI (16 mg, 0.084 mmol) and $R^1C{\equiv}CH$ (80.0 mmol). After being stirred at 80°C for 5 h, the mixture was cooled, filtered and concentrated. Water was added to the residue followed by Et_2O. Phases were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were washed several times with H_2O and eventually dried over Na_2SO_4. After removal of the solvent by rotary evaporation, the crude product was purified by column chromatography on silica gel using as eluent 9:1 hexane/AcOEt (R^1=Bu: 8.6 g, 85%; R^1=Ph: 9.4 g, 84%). Spectroscopic properties of aldehydes thus obtained agreed with those reported.[14]

To a stirred solution of the aldehyde (45 mmol) in anhydrous THF (450 mL) was added dropwise at 0°C 18.0 mL of a 2 M solution of BuLi in pentane (36 mmol). After being stirred at 0°C for 2 h, the mixture was quenched with ice-water and then with a 10% solution of HCl to neutral pH. Phases were separated, and the aqueous layer extracted with Et_2O. The combined organic layers were washed with H_2O and brine, and then dried over Na_2SO_4. After removal of the solvent by rotary evaporation, the crude product was purified by column chromatography on silica gel using as eluent 8:2 hexane/AcOEt: **1c** was a pale yellow oil (6.6 g, 60% with respect to starting aldehyde), **1f** was a yellow oil (7.1 g, 60% with respect to starting aldehyde).

4.6. Coupling between methyl 2-iodobenzoate and alk-1-ynes followed by addition of EtMgBr

Methyl 2-iodobenzoate was prepared by Fischer esterification of 2-iodobenzoic acid, according to the general procedure described by Vogel.[15] Thus, to a solution of 2-iodobenzoic acid (25 g, 0.1 mol) in MeOH (41 mL, 1.0 mol) was added 6.0 mL of conc. H_2SO_4. The mixture was refluxed in air for 2.5 h, and then it was cooled, diluted with H_2O (200 mL) and extracted several times with $CHCl_3$. The combined organic layers were washed with H_2O, 5% $NaHCO_3$ (2 times), H_2O again, and brine (2 times), and eventually dried over Na_2SO_4. Removal of the solvent by rotary evaporation afforded crude methyl 2-iodobenzoate as a colorless oil, which was sufficiently pure for the next step (23.3 g, 89%). The method of Shi[16] and Zhang[17] was employed for the coupling. To a stirred solution of the above ester (10.2 g, 38.9 mmol) in anhydrous DMF (195 mL) were added $Pd(PPh_3)_2Cl_2$ (2.74 g, 3.9 mmol), CuI (742 mg, 3.9 mmol), $(i\text{-}Pr)_2NEt$ (21 mL) and $R^1C{\equiv}CH$ (78 mmol). The mixture was allowed to stir at rt for 18 h, and then sat. NH_4Cl (200 mL) and hexane (200 mL) were added and phases separated. The aqueous layer was extracted with hexane, and the combined organic layers were washed with H_2O and brine, and then dried over Na_2SO_4. After removal of the solvent by rotary evaporation, the crude product was purified by column chromatography on silica gel using as eluent 9:1 hexane–AcOEt. Methyl 2-hex-1-ynylbenzoate (R^1=Bu) was a yellow oil (8.1 g, 96%); methyl 2-phenylethynylbenzoate (R^1=Ph) was a yellow oil, 8.8 g, 96%).

To a stirred solution of EtMgBr [78 mmol, prepared in anhydrous Et_2O (33 mL) from 1.9 g of Mg (78 mmol) and 8.8 g of EtBr (81 mmol)] was added dropwise a solution of the alkynyl ester (37 mmol) in anhydrous benzene (17 mL) with cooling. The mixture was then refluxed with stirring for 1 h. After cooling, a mixture of ice (85 g) and conc. HCl (1.9 mL) was slowly added with external cooling, followed by the addition of NH_4Cl (2.86 g) and Et_2O. Phases were separated, and the organic layer was washed with water, 5% $NaHCO_3$, and water again. After drying over Na_2SO_4, solvent was removed by rotary evaporation and the crude product purified by column chromatography on silica gel using as eluent 95:5 hexane–AcOEt: **1d** was a pale yellow oil (5.4 g, 60%), **1g** was a yellow oil (7.1 g, 73%).

4.7. General procedure for cycloisomerization reactions

Reactions were carried out on a 3–5 mmol scale based on 2-alkynylbenzyl alcohol **1**. Solvent, substrate: PdI_2 molar ratio, reaction temperature and time, yield of products **2**, **3** and **4a** are indicated in Tables 1–5. In a typical experiment, PdI_2 and KI (2 mol per mol of palladium) were added to a solution of **1** in the suitable anhydrous solvent in a Schlenk flask. The resulting mixture was stirred at the temperature and for the time required to obtain a satisfactory conversion, as shown by GLC and/or TLC analysis (Tables 1–5).

4.8. Separation of products

After removal of the reaction solvent by rotary evaporation, products were isolated by column chromatography on silica gel (**2e** and **f**, **3b**–**f**, and **4a**) or on neutral alumina under nitrogen (**2d**, **2g**; these products underwent decomposition by using silica gel in the presence of air). Products **3d** (pale yellow oil), **2d** (yellow oil) were eluted in this order using hexane as eluent. Products **3e** (colorless solid), **2e** (colorless solid) were eluted in this order using pure hexane as eluent. Products **3f** (yellow oil), **2f** (yellow oil) were eluted in this order using 9:1 hexane/AcOEt as eluent. **2g** (colorless solid) was eluted using 98:2 hexane/AcOEt. **3b** (pale yellow oil) was eluted using 98:2 hexane/AcOEt. **3c** (pale yellow oil) was eluted using 9:1 hexane/AcOEt. **4a** (sticky yellow oil) was eluted using 9:1 hexane/AcOEt.

4.9. Characterization of substrates and products

All substrates and products were fully characterized by spectroscopic techniques and elemental analysis. Compounds **1a**[4,5,18] (mp=66–67°C), **1e**[4,5,19] (mp 72–73°C), **2e**[4,5] (mp 100–102°C), **3e**[20] (mp 123–125°C), were characterized by comparison with literature data. Characterization data for new compounds and for compounds previously not fully characterized are reported below.

4.9.1. (2-Trimethylsilanylethynylphenyl)methanol 1a′.[5,19] Pale yellow oil. IR (neat) 3350 (m, br), 2959 (m), 2155 (m), 1480 (w), 1450 (w), 1249 (m), 1041 (m), 867 (s), 843 (s), 759 (m), 646 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46–7.36 (m, 2H on phenyl ring, H-3+H-6), 7.29 (td, J=7.6, 1.5 Hz, 1H, H-4 or H-5), 7.19 (td, J=7.6, 1.5 Hz, 1H, H-5 or H-4), 4.78

(s, 2H, CH_2), 0.26 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$) δ 143.3, 132.5, 129.0, 127.3, 127.1, 121.2, 102.8, 99.6, 63.9, 0.05; MS *m/e* 204 (35, M^+), 189 (16) 171 (22), 145 (16), 131 (42), 129 (52), 128 (35), 115 (32), 75 (19), 73 (52), 61 (100). Anal. calcd for $C_{12}H_{16}OSi$ (FW 204.34): C, 70.53; H, 7.89. Found C, 70.71; H, 7.87.

4.9.2. (2-Hex-1-ynylphenyl)methanol 1b.[19] Pale yellow oil. IR (neat) 3347 (m, br), 2956 (s), 2929 (s), 2871 (m), 2227 (w), 1452 (m), 1041 (m), 757 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.36 (m, 2H on phenyl ring), 7.31–7.18 (m, 2H on phenyl ring), 4.79 (s, 2H, CH_2), 2.45 (t, *J*=6.9 Hz, 2H, $CH_2C{\equiv}$), 1.67–1.55 (m, 2H, $CH_2CH_2CH_3$), 1.55–1.42 (m, 2H, $CH_2CH_2CH_3$), 0.95 (t, *J*=7.3 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) δ 142.4, 131.9, 127.7, 127.0, 126.8, 122.0, 95.2, 78.1, 63.7, 30.7, 21.9, 19.0, 13.4; MS *m/e* 188 (27, M^+), 155 (32), 145 (71), 131 (46), 129 (35), 128 (41), 127 (23), 117 (49), 116 (26), 115 (100), 91 (54), 77 (25). Anal. calcd for $C_{13}H_{16}O$ (FW 188.27): C, 82.94; H, 8.57. Found C, 83.14; H, 8.59.

4.9.3. 1-(2-Hex-1-ynylphenyl)pentan-1-ol 1c. Pale yellow oil. IR (neat) 3344 (m, br), 2955 (s), 2930 (s), 2870 (w), 2859 (w), 2228 (vw), 1465 (w), 1049 (m), 758 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45–7.40 (m, 1H on phenyl ring, H-3 or H-6), 7.35 (dd, *J*=7.3 1.5 Hz, 1H, H-6 or H-3), 7.25 (td, *J*=7.3, 1.5 Hz, 1H on phenyl ring, H-4 or H-5), 7.14 (td, *J*=7.3, 1.5 Hz, 1H on phenyl ring, H-5 or H-4), 5.08 (dd, *J*=7.3, 5.4 Hz, 1H, $CHCH_2$), 2.43 (t, *J*=6.8 Hz, 2H, $CH_2C{\equiv}$), 1.85–1.25 (m, 10H, $CHCH_2CH_2CH_2{+}{\equiv}CCH_2CH_2CH_2CH_3$), 0.95 (t, *J*=7.3 Hz, 3H, Me), 0.89 (t, *J*=6.8 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) δ 146.8, 132.2, 127.9, 126.7, 125.3, 121.4, 95.3, 78.5, 72.4, 37.9, 30.9, 28.2, 22.6, 22.1, 19.2, 14.1, 13.6; MS *m/e* 244 (5, M^+), 188 (16), 187 (100), 145 (16), 141 (13), 131 (17), 129 (11), 128 (11), 117 (25), 115 (27), 91 (10). Anal. calcd for $C_{17}H_{24}O$ (FW 244.37): C, 83.55; H, 9.90. Found C, 83.78; H, 9.87.

4.9.4. 3-(2-Hex-1-ynylphenyl)pentan-3-ol 1d. Pale yellow oil. IR (neat) 3498 (m, br), 2961 (s), 2932 (s), 2874 (m), 2225 (vw), 1462 (m), 1159 (m), 959 (m), 758 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45 (dd, *J*=7.6, 1.5 Hz, 1H on phenyl ring, H-3 or H-6), 7.42 (dd, *J*=7.6, 1.5 Hz, 1H on phenyl ring, H-6 or H-3), 7.24 (td, *J*=7.6, 1.5 Hz, 1H on phenyl ring, H-4 or H-5), 7.14 (td, *J*=7.6, 1.5 Hz, 1H on phenyl ring, H-5 or H-4), 2.44 (t, *J*=7.1 Hz, 2H, $CH_2C{\equiv}$), 2.37–2.23 [m, 2H, $(CH_3CHH)_2COH$], 1.97–1.83 [m, 2H, $(CH_3CHH)_2COH$], 1.66–1.54 (m, 2H, $CH_2CH_2CH_3$), 1.54–1.41 (m, 2H, $CH_2CH_2CH_3$), 0.95 (t, *J*=7.3 Hz, 3H, $CH_2CH_2CH_3$), 0.77 [t, *J*=7.3 Hz, 6H, $(CH_3CH_2)_2COH$]; ^{13}C NMR ($CDCl_3$) δ 146.7, 134.6, 127.4, 126.9, 126.1, 120.3, 96.2, 80.8, 78.4, 32.8, 30.6, 22.1, 19.3, 13.6, 8.1; MS *m/e* 244 (1, M^+), 216 (16), 215 (100), 201 (3), 172 (6), 159 (5), 157 (8), 141 (4), 129 (6), 128 (8), 115 (9), 91 (2), 57 (8). Anal. calcd for $C_{17}H_{24}O$ (FW 244.37): C, 83.55; H, 9.90. Found C, 83.64; H, 9.92.

4.9.5. 1-(2-Phenylethynylphenyl)pentan-1-ol 1f. Yellow oil. IR (neat) 3356 (m, br), 2955 (m), 2930 (m), 2869 (w), 2858 (w), 2215 (vw), 1493 (m), 1444 (w), 1047 (w), 1029 (w) 756 (s), 690 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53–7.45 (m, 4H on phenyl ring), 7.36–7.27 (m, 4H on phenyl ring), 7.19 (td, *J*=7.6, 1.5 Hz, 1H on phenyl ring), 5.21 (dd, *J*=7.8, 5.4 Hz, 1H, $CHOH$), 1.91–1.68 (m, 2H, $CHOHCH_2$), 1.56–1.24 (m, 4H, $CH_2CH_2CH_3$), 0.86 (t, *J*=7.1, 3 Hz, Me); ^{13}C NMR ($CDCl_3$) δ 147.0, 132.1, 131.4, 128.7, 128.4, 126.9, 125.4, 123.2, 120.5, 94.1, 87.3, 72.2, 38.1, 28.1, 22.6, 14.1; MS *m/e* 264 (17, M^+), 221 (21), 208 (21), 207 (100), 179 (29), 178 (65), 176 (13), 152 (9). Anal. calcd for $C_{19}H_{20}O$ (FW 264.36): C, 86.32; H, 7.63. Found C, 86.15; H, 7.64.

4.9.6. 3-(2-Phenylethynylphenyl)pentan-3-ol 1g. Yellow oil. IR (neat) 3518 (m, br), 2967 (m), 2934 (m), 2877 (w), 2213 (vw), 1491 (m), 1442 (w), 1160 (m), 959 (m), 756 (s), 690 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63–7.46 (m, 4H on phenyl ring), 7.39–7.28 (m, 4H on phenyl ring), 7.21 (td, *J*=7.3, 1.5 Hz, 1H on phenyl ring), 2.56–2.42 [m, 2H, $(CH_3CHH)_2COH$], 2.04–1.88 [m, 2H, $(CH_3CHH)_2COH$], 0.79 [t, *J*=7.3 Hz, 6H, $(CH_3CH_2)_2COH$]; ^{13}C NMR ($CDCl_3$) δ 147.0, 134.4, 131.1, 128.45, 128.41, 128.2, 127.1, 126.3, 123.2, 119.4, 94.4, 89.7, 78.4, 33.1, 8.1; MS *m/e* 264 (5, M^+), 236 (19), 235 (100), 220 (9), 202 (6), 191 (7), 176 (5), 91 (3). Anal. calcd for $C_{19}H_{20}O$ (FW 264.36): C, 86.32; H, 7.63. Found C, 86.48; H, 7.61.

4.9.7. (*Z*)-1,1-Diethyl-3-pentylidene-1,3-dihydroisobenzofuran 2d. Yellow oil. IR (neat) 2964 (s), 2930 (s), 2874 (m), 2853 (w), 1679 (m), 1463 (s), 1354 (w), 1296 (m), 1050 (m), 752 (s) cm^{-1}; ^1H NMR (benzene-d_6) δ 7.27–7.22 (m, 1H on aromatic ring), 7.06–7.01 (m, 2H on aromatic ring), 6.78–6.72 (m, 1H on aromatic ring), 4.94 (t, *J*=7.3 Hz, 1H, =CH), 2.54 (q, *J*=7.3 Hz, 2H, $CH_2CH{=}$), 1.94–1.80 (m, 2H, 2 $OCCHHCH_3$), 1.76–1.37 (m, 6H, 2 $OCCHHCH_3{+}CH_2CH_2CH_3$), 0.95 (t, *J*=7.3 Hz, 3H, $CH_2CH_2CH_2CH_3$), 0.74 (t, *J*=7.3 Hz, 6H, 2 $OCCH_2CH_3$); MS *m/e* 244 (13, M^+), 216 (18), 215 (100), 201 (41), 173 (8), 159 (12), 157 (12), 145 (12), 128 (10), 115 (10), 91 (5), 57 (6). Anal. calcd for $C_{17}H_{24}O$ (FW 244.37): C, 83.55; H, 9.90. Found C, 83.71; H, 9.87.

4.9.8. (*Z*)-1-Benzylidene-3-butyl-1,3-dihydroisobenzofuran 2f. Yellow oil. IR (neat) 2955 (m), 2929 (m), 2869 (m), 1655 (s), 1464 (m), 1365 (m), 1307 (w), 1049 (s), 809 (w), 761 (s), 693 (m), 517 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.78–7.72 (m, 2H on aromatic ring), 7.53–7.47 (m, 1H on aromatic ring), 7.36–7.23 (m, 4H on aromatic ring), 7.22–7.16 (m, 1H on aromatic ring), 7.16–7.09 (m, 1H on aromatic ring), 5.88 (s, 1H, =CH), 5.60 (dd, *J*=7.8, 3.9 Hz, 1H, OCH), 2.03–1.89 (m, 1H, $CHHCH_2CH_2CH_3$), 1.82–1.67 (m, 1H, $CHHCH_2CH_2CH_3$), 1.57–1.29 (m, 4H, $CH_2CH_2CH_2CH_3$), 0.90 (t, *J*=7.3 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) δ 155.5, 142.7, 136.7, 135.0, 128.6, 128.3, 128.1, 127.7, 125.1, 121.2, 119.9, 95.7, 86.1, 35.7, 27.1, 22.6, 14.0; MS *m/e* 264 (60, M^+), 221 (17), 208 (20), 207 (100), 179 (15), 178 (40), 115 (11), 91 (7). Anal. calcd for $C_{19}H_{20}O$ (FW 264.36): C, 86.32; H, 7.63. Found C, 86.17; H, 7.65.

4.9.9. (*Z*)-3-Benzylidene-1,1-diethyl-1,3-dihydroisobenzofuran 2g. Colorless solid, mp 61–62°C. IR (KBr) 2960 (w), 1649 (m), 1462 (m), 1358 (w), 1096 (w), 1051 (m), 939 (s), 820 (m), 761 (s), 696 (s), 522 (m) cm^{-1}; ^1H NMR (benzene-d_6) δ 8.04–7.99 (m, 2H on aromatic ring), 7.39–7.31 (m, 2H on aromatic ring), 7.27–7.20 (m, 1H on aromatic ring), 7.13–6.99 (m, 3H on aromatic ring),

6.74–6.67 (m, 1H on aromatic ring), 5.96 (s, 1H, =CH), 1.93–1.79 (m, 2H, 2 C*H*HCH$_3$), 1.67–1.53 (m, 2H, 2 CH*H*CH$_3$), 0.68 (t, *J*=7.3 Hz, 6H, 2 Me); ^{13}C NMR (benzene-d_6) δ 155.9, 144.4, 137.5, 136.6, 128.7, 128.4, 128.1, 125.4, 121.0, 120.0, 96.0, 94.7, 33.0, 7.8; MS *m/e* 264 (27, M$^+$), 236 (19), 235 (100), 220 (6), 202 (4), 191 (7). Anal. calcd for $C_{19}H_{20}O$ (FW 264.36): C, 86.32; H, 7.63. Found C, 86.46; H, 7.63.

4.9.10. 3-Butyl-1*H*-isochromene 3b.[5] Pale yellow oil. IR (neat) 2956 (s), 2929 (m), 2869 (w), 2859 (w), 1644 (s), 1488 (m), 1454 (m), 1392 (w), 1154 (m), 1025 (m), 799 (m), 750 (m) cm^{-1}; ^{1}H NMR (acetone-d_6) δ 7.15 (tdt, *J*=7.3, 1.7, 0.6 Hz, 1H on aromatic ring), 7.07 (td, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 7.03–6.99 (m, 1H on aromatic ring), 6.91 (dd, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 5.69 (s, br, 1H, =CH), 5.01 (s, 2H, OCH$_2$), 2.17 (td, *J*=7.4, 0.6 Hz, 2H, CH$_2$C=), 1.58–1.47 (m, 2H, C*H*$_2$CH$_2$CH$_3$), 1.43–1.29 (m, 2H, CH$_2$C*H*$_2$CH$_3$), 0.91 (t, *J*=7.3 Hz, 3H, Me); ^{13}C NMR (acetone-d_6) δ 159.6, 132.9, 128.7, 128.2, 126.4, 124.4, 123.0, 101.6, 69.1, 33.8, 30.0, 22.8, 14.1; MS *m/e* 188 (83, M$^+$), 187 (39), 146 (48), 145 (27), 131 (28), 117 (36), 115 (35), 104 (100), 103 (40), 91 (16), 77 (24). Anal. calcd for $C_{13}H_{16}O$ (FW 188.27): C, 82.94; H, 8.57. Found C, 83.08; H, 8.60.

4.9.11. 1,3-Dibutyl-1*H*-isochromene 3c. Pale yellow oil. IR (neat) 2955 (s), 2930 (s), 2869 (w), 2859 (w), 1648 (m), 1488 (w), 1465 (w), 1454 (m), 1381 (m), 1155 (m), 795 (m), 748 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.13 (td, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 7.06 (td, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 6.92 (dd, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 6.88 (dd, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 5.55 (s, br, 1H, =CH), 5.04 (dd, *J*=8.8, 4.9 Hz, 1H, OCH), 2.17 (td, *J*=7.6, 1.0 Hz, 2H, CH$_2$C=), 2.05–1.91 (m, 1H, OCHC*H*H), 1.73–1.27 (m, 9H, OCHCH*H*+2C*H*$_2$C*H*$_2$-CH$_3$), 0.92 (t, *J*=7.3 Hz, 3 H, Me), 0.91 (t, *J*=7.1 Hz, 3 H, Me); ^{13}C NMR (CDCl$_3$) δ 156.4, 131.2, 130.8, 127.6, 125.4, 123.8, 122.6, 99.9, 77.9, 33.8, 33.7, 29.1, 27.5, 22.6, 22.3, 14.0, 13.9; MS *m/e* 244 (10, M$^+$), 188 (15), 187 (100), 115 (9). Anal. calcd for $C_{17}H_{24}O$ (FW 244.37): C, 83.55; H, 9.90. Found C, 83.78; H, 9.91.

4.9.12. 3-Butyl-1,1-diethyl-1*H*-isochromene 3d. Pale yellow oil. IR (neat) 2963 (s), 2933 (s), 2875 (w), 1656 (m), 1455 (m), 1377 (m), 1149 (m), 791 (m), 748 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.09 (td, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 7.03 (td, *J*=7.3, 2.0 Hz, 1H on aromatic ring), 6.88 (dd, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 6.84 (dd, *J*=7.3, 2.0 Hz, 1H on aromatic ring), 5.38 (s, 1H, =CH), 2.14 (t, *J*=7.3 Hz, 2H, CH$_2$C=), 1.97–1.77 (m, 4H, 2 OCC*H*$_2$-CH$_3$), 1.62–1.49 (m, 2H, C*H*$_2$CH$_2$CH$_3$), 1.44–1.30 (m, 2H, CH$_2$C*H*$_2$CH$_3$), 0.92 (t, *J*=7.3 Hz, 3H, CH$_2$CH$_2$C*H*$_3$), 0.85 (t, *J*=7.3 Hz, 6H, 2 OCCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$) δ 156.1, 132.0, 131.9, 127.1, 125.2, 124.0, 122.9, 98.0, 83.9, 33.9, 31.8, 28.9, 22.4, 13.9, 8.1; MS *m/e* 244 (7, M$^+$), 216 (17), 215 (100), 172 (4), 128 (6), 115 (6). Anal. calcd for $C_{17}H_{24}O$ (FW 244.37): C, 83.55; H, 9.90. Found C, 83.45; H, 9.92.

4.9.13. 1-Butyl-3-phenyl-1*H*-isochromene 3f. Yellow oil. IR (neat) 2954 (s), 2930 (s), 2850 (w), 1491 (m), 1453 (m), 1376 (w), 1278 (w), 1059 (m), 763 (s), 690 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.78–7.71 (m, 2H on aromatic ring), 7.44–7.26 (m, 3H on aromatic ring), 7.20 (td, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 7.14 (td, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 7.06 (distorted dd, *J*=7.3, 1.5 Hz, 1H on aromatic ring), 7.03–6.98 (m, 1H on aromatic ring), 6.39 (s, 1H, =CH), 5.23 (dd, *J*=8.8, 4.4 Hz, 1H, OCH), 2.15–1.99 (m, 1H, C*H*HCH$_2$CH$_2$CH$_3$), 1.84–1.70 (m, 1H, CH*H*CH$_2$CH$_2$-CH$_3$), 1.70–1.27 (m, 4H, C*H*$_2$C*H*$_2$CH$_3$), 0.91 (t, *J*=7.3 Hz, 3H, Me); ^{13}C NMR (CDCl$_3$) δ 151.6, 134.7, 131.7, 131.0, 128.6, 128.3, 127.7, 126.3, 125.0, 123.84, 123.78, 100.3, 78.2, 33.5, 27.6, 22.5, 14.1; MS *m/e* 264 (15, M$^+$), 208 (16), 207 (100), 178 (22). Anal. calcd for $C_{19}H_{20}O$ (FW 264.36): C, 86.32; H, 7.63. Found C, 86.13; H, 7.65.

4.9.14. Spiro compound 4a. Sticky yellow oil. IR (neat) 1695 (m), 1487 (w), 1451 (w), 1354 (w), 1251 (w), 1108 (w), 1027 (m), 786 (s), 760 (s) cm^{-1}; ^{1}H NMR (CD$_3$OD) δ 7.65–7.60 (m, 1H on phenyl ring), 7.54–7.10 (m, 6H on phenyl ring), 7.10–7.03 (m, 1H on phenyl ring), 4.98 (s, 1H, OCH), 4.90 (s, OCH$_2$), 2.50 (s, 2H, CCH$_2$C), 1.97 (s, 3H, Me); MS *m/e* 264 (100, M$^+$), 249 (47), 231 (45), 222 (18), 221 (20), 207 (22), 203 (22), 202 (19), 193 (22), 178 (42), 147 (23), 132 (39), 115 (55), 91 (41), 77 (21). Anal. calcd for $C_{18}H_{16}O_2$ (FW 264.32): C, 81.79; H, 6.10. Found C, 81.99; H, 6.08.

4.9.15. Methyl 2-hex-1-ynylbenzoate. Yellow oil. IR (neat) 2955 (m), 2931 (m), 2229 (w), 1733 (s), 1484 (w), 1447 (w), 1432 (w), 1295 (m), 1250 (s), 1129 (m), 1083 (m), 757 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.86 (dd, *J*=7.6, 1.5 Hz, 1H on phenyl ring, H-6), 7.49 (dd, *J*=7.6, 1.5 Hz, 1H, H-3), 7.39 (td, *J*=7.6, 1.5 Hz, 1H on phenyl ring, H-4 or H-5), 7.28 (td, *J*=7.6, 1.5 Hz, 1H on phenyl ring, H-5 or H-4), 3.90 (s, 3H, CO$_2$Me), 2.47 (t, *J*=6.8 Hz, 2H, CH$_2$C≡), 1.68–1.43 (m, 4H, C*H*$_2$C*H*$_2$CH$_3$), 0.95 (t, *J*=7.1 Hz, 3H, CH$_2$CH$_3$); ^{13}C NMR (CDCl$_3$) δ 167.0, 134.2, 132.0, 131.5, 130.1, 127.1, 124.5, 96.0, 79.3, 52.0, 30.8, 22.1, 19.5, 13.7; MS *m/e* 216 (8, M$^+$), 201 (12), 185 (10), 174 (100), 159 (38), 155 (15), 143 (16), 131 (16), 115 (26). Anal. calcd for $C_{14}H_{16}O_2$ (FW 216.28): C, 77.75; H, 7.46. Found C, 77.66; H, 7.47.

4.9.16. Methyl 2-phenylethynylbenzoate.[21] Yellow oil. IR (neat) 3061 (w), 2949 (w), 2217 (w), 1729 (s), 1493 (m), 1293 (s), 1252 (s), 1128 (m), 1078 (m), 756 (s), 691 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.96 (dd, *J*=7.8, 1.5 Hz, 1H on phenyl ring, H-6), 7.65–7.55 (m, 3H on phenyl ring), 7.45 (td, *J*=7.6, 1.5 Hz, 1H on phenyl ring), 7.38–7.30 (m, 4H on phenyl ring), 3.94 (s, 3H, CO$_2$Me); ^{13}C NMR (CDCl$_3$) δ 166.6, 133.9, 131.73, 131.68, 130.5, 128.5, 128.3, 127.9, 123.7, 123.3, 94.4, 88.3, 52.1; MS *m/e* 236 (100, M$^+$), 221 (63), 207 (18), 205 (26), 193 (24), 177 (18), 176 (46), 165 (41), 151 (16), 150 (15), 122 (22), 105 (23), 88 (26), 77 (18). Anal. calcd for $C_{16}H_{12}O_2$ (FW 236.27): C, 81.34; H, 5.12. Found C, 81.12; H, 5.11.

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