Reaction of 4-Chlorocoumarin with Organometallic Reagents. Synthesis of Trialkylbenzopyrans, 4-Chlorobenzopyrans, 4-Alkylcoumarins and *o*-Hydroxyphenylprop-2-ynyl Alcohols

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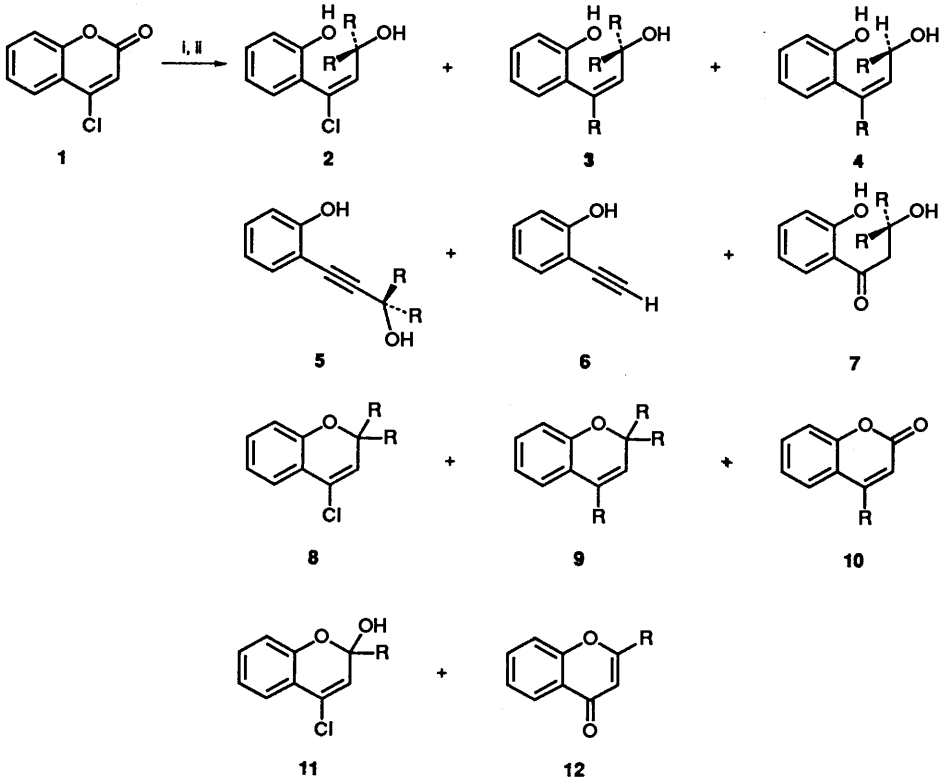
4-Chlorocoumarin has been shown to be a highly versatile starting material when treated with organometallic reagents. Thus, it has allowed the selective synthesis either directly, or through simple additional transformations, of 4-alkylcoumarins (with R_2CuLi in Et_2O, or Pr^iMgBr in THF), 2-chloro-2-(*o*-hydroxyphenyl)allyl alcohols or their 4-chloro-2*H*-1-benzopyran derivatives (with RMgX in THF), 2-(*o*-hydroxyphenyl)prop-2-ynyl alcohols (when non-acid hydrolysis were used in the latter reactions) and 2,2,4-trialkyl-2*H*-1-benzopyrans (when excess of RMgX or R_3Al reagents were used).

As a part of a more general project directed to the synthesis of halogeno-2*H*-1-benzopyrans, we have studied the behaviour of the 4-chlorocoumarin **1** towards organometallic reagents. The presence of the halogen at C-4 modifies the reactivity of the heterocycle, making it more sensitive to variations in experimental conditions than are the 3-halogenocoumarins.[1] The reaction of 4-chlorocoumarin with organometallic derivatives (RMgX, R_3Al, RLi, R_2CuLi) can lead to a complex mixture of compounds (Scheme 1), depending on the nature of the organometallic reagent, the reaction and the hydrolysis conditions.

Reactions with Magnesium Derivatives.—Primary alkylmagnesium halides (R = methyl, ethyl, propyl or butyl) allowed selective preparation of compound **2** or **3**. Thus, when the reactions were carried out in THF (tetrahydrofuran), at 0 °C for a maximum of 1 h, and molar ratio RMgX/**1**, 5/1, a good yield (72–89%) of compound **2** was obtained, whereas the transformation of compound **2** into compound **3** was observed (except for MeMgI) when longer reaction times were used. However, in toluene, diethyl ether or THF at 25 °C, for one hour or more and molar ratio 8/1, the major product was compound **3**, which was obtained in moderate to very good yield (51–83%). Complex mixtures of products were obtained when different experimental conditions were employed (Table 1). Nevertheless, the isolation and purification of compound **2** was possible only by recrystallization from the crude reaction mixture where they were formed in high yield. Attempts at purification by other methods (including flash chromatography) transformed compound **2** into dehydrochlorination **5**, or cyclization **8** products. This behaviour was also observed for compounds **3**, which autotransformed readily into 2,2,4-trialkyl-2*H*-1-benzopyrans **9**. It is noteworthy that the hydrolytic conditions are crucial to obtain **2** and **3** in good yields; thus using cold saturated aqueous NH_4Cl (or a very dilute acidic solution and ice) followed by



Scheme 1 **a** R = H, **b** R = Me, **c** R = Et, **d** R = Pr, **e** R = Bu, **f** R = Pr^i, **g** R = Bu^i. *Reagents:* i, RM; ii, H_2O.

Table 1 Reaction of compound **1** with Grignard derivatives

RMgX	Solvent	T/°C	t/h	1/RM	Product (% Yield) 2	3	10	5[b]
MeMgI	PhMe	0	2	1/8	**2b** (5)			**5b** (68)
	Et_2O	0	2	1/8	**2b** (65)			**5b** (10)
	THF	0	2	1/8	**2b** (85)			
EtMgI	PhMe	25	2	1/8		**3c** (75)		**5c** (10)
	Et_2O	25	2	1/8	**2c** (30)	**3c** (41)		
	THF	0	2	1/8	**2c** (42)			**5c** (30)
EtMgBr	PhMe	25	1	1/8		**3c** (71)		**5c** (10)
	Et_2O	25	1	1/8		**3c** (81)		**5c** (7)
	THF	25	1	1/8		**3c** (68)		
	THF	0	1	1/5	**2c** (75)	**3c** (7)		
	THF[b]	0	1	1/8				**5c** (70)
PrMgBr	PhMe	25	1	1/8		**3d** (75)		**5d** (17)
	PhMe	0	1	1/8	**2d** (48)	**3d** (25)		**5d** (10)
	Et_2O	25	1	1/8	**2d**(7)	**3d** (80)		**5d** (5)
	Et_2O	0	1	1/8	**2d** (64)	**3d** (30)		
	THF	25	0.5	1/5	**2d** (45)	**3d** (30)		**5d** (12)
	THF	0	1	1/5	**2d** (72)	**3d** (10)		
	THF[b]	0	1	1/5				**5d** (65)
BuMgBr	PhMe	25	1	1/8		**3e** (83)		**5e** (8)
	PhMe[b]	0	1	1/5		**3e** (20)		**5e** (58)
	Et_2O	25	1	1/8		**3e** (60)		**5e** (21)
	THF	25	1	1/8		**3e** (51)		**5e** (35)
	THF	0	1	1/5	**2e** (89)			
Pr^iMgBr	PhMe	25	1	1/8	**2f** (79)		**10f** (5)	
	PhMe	0	1	1/8	**2f** (85)			
	Et_2O	25	0.5	1/8	**2f** (35)	**3f** (30)		**5f** (28)
	Et_2O	−50[c]	20	1/8	**2f** (5)	**3f** (79)		
	Et_2O	0	1	1/8	**2f** (75)			
	THF	25	0.5	1/8	**2f** (30)	**3f** (50)		
	THF	−50[c]	20	1/8		**3f** (75)		
	THF	0	1	1/8	**2f** (49)	**3f** (40)		
	THF[b]	0	1	1/8				**5f** (65)
	THF[d]	25	1	1/8			**10f** (79)	
	Et_2O	−50	0.5	1/8			**10f** (80)	
	THF	−50	0.5	1/8			**10f** (69)	

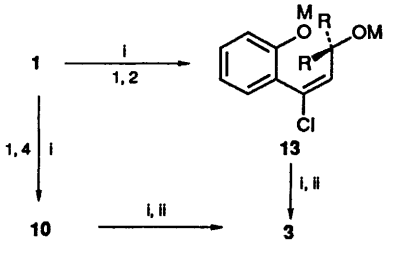
[a] Yields in all tables were calculated from NMR spectra of the reaction mixture. [b] Aqueous hydrolysis. [c] 30 min at −50 °C, and then allowed to warm to room temp. [d] Test negative (THF–benzophenone–Na, colourless solution).

immediate work-up and removal of the solvent under reduced pressure at room temp. allowed the syntheses of the mentioned products.

The behaviour of isopropylmagnesium bromide towards **1** was different from that shown by primary magnesium derivatives. The most important difference is the possibility to obtain 4-alkylcoumarin **10f** (1,4-addition–elimination) in very good yield (69–80%), in diethyl ether or THF at −50 °C. In this case the bis-addition was the predominant process at temperatures higher than 0 °C, and the best yield (85%) for **2f** was obtained in toluene, instead of THF. The reason for this behaviour is that the competing 1,4-addition process does not take place in this solvent,[1–5] and the lower reactivity of the isopropylmagnesium bromide allows a better control of the reaction leading to compound **13** (Scheme 2).

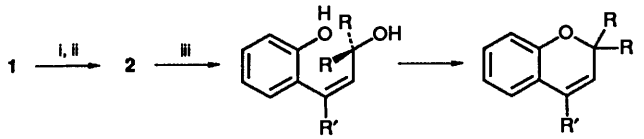
Unfortunately, other secondary alkylmagnesium derivatives, such as sec-butyl- or cyclopentyl-magnesium bromides yielded 4-alkyl coumarins in very low yields.

Monitoring of the reactions showed that trialkyl derivatives **3** may be obtained either through **10** (for Pr^iMgBr), or through the alkoxides **13** (for RMgBr; R = Et, Pr, Bu) (Scheme 2). The latter possibility opened a versatile path to trisubstituted benzopyrans with different alkyl groups attached to C-2 and C-4. Thus, these substrates can be obtained from compound **1** simply by appropriately changing the organometallic reagent used in each step (Scheme 3) (Table 2).



Scheme 2 *Reagents:* i, RM; ii, H_2O

On the other hand, although 3-(*o*-hydroxyphenyl)prop-2-ynyl alcohols **5** could be formed by dehydrohalogenation during the reaction,[6] their ratios in the final mixtures are highly dependent on the conditions of hydrolysis. Thus, derivatives **5** were obtained as major compounds (58–79%) (after column chromatography) when the reactions were hydrolysed only by water, whereas quenching the reaction mixture with acetic acid



3 R = R′ **9** R = R′
14 R = Et, R′ = Bu **15** R = Et, R′ = Bu
16 R = Bu, R′ = Et **17** R = Bu, R′ = Et

Scheme 3 *Reagents:* i, RMgX; ii, H_2O; iii, R′MgX

Table 2 Reaction of compounds **2** with RM

2	RM	Solvent[a]	t/h	Product (% yield)
2b	Me_3Al	CH_2Cl_2	20	**9b** (40)
2c	EtMgBr	Et_2O	12	**3c** (70)
2c	Et_3Al	PhMe	20	**3c** (65)
2c	BuMgBr	Et_2O	12	**14** (72)
2e	BuMgBr	Et_2O	12	**3e** (72)
2e	BuMgBr	PhMe	12	**3e** (76)
2e	EtMgBr	Et_2O	12	**16** (68)
2e	Bu_3Al	PhMe	20	**3e** (60)

[a] The reactions were carried out at 25 °C; molar ratio **2**/RM: 1/4.

Table 3 Reaction of compound **1** with R_3Al

RM	Solvent[a]	T/°C[a]	1/RM	Products (% yield)
Me_3Al	PhMe	25	1/6	**3b** (—)
	CH_2Cl_2	25	1/6	**9b** (49)
	CH_2Cl_2	25	1/8	**9b** (65)
Et_3Al	PhMe	0	1/6	**3c** (72)
	PhMe	25	1/6	**3c** (85)
	CH_2Cl_2	25	1/6	**9c** (60)
	CH_2Cl_2	−50[b]	1/6	**9c** (75)
	Et_2O	25	1/6	**3c** (—)
	THF	25	1/6	**3c** (—)
Bu_3Al	PhMe	−50[b]	1/6	**3e** (85)
	PhMe	0	1/6	**3e** (75)
	PhMe	25	1/6	**3e** (67)
Bu^i_3Al	PhMe	−50[b]	1/6	**2a** (34), **4g** (52)
	PhMe	0	1/6	**2a** (25), **4g** (60)
	PhMe	25	1/6	**2a** (10), **4g** (65)
Bu^i_2Al-H	PhMe	−50	1/6	**2a** (78)
	PhMe	−50	1/2.5	**11a** (80)
	PhMe	25	1/3	**2a** (75)
	Et_2O	−50	1/2.5	**11a** (40), **1** (45)

[a] The reactions were carried out for 20 h. [b] 30 min at −50 °C, and then allowed to warm to room temp.

led to mixtures of compounds **2**, **8** and, in some cases, **7**. These results suggest that the dehydrohalogenation process mainly occurs during, or after, hydrolysis in non-acidic conditions.

Reactions with Organoaluminium Derivatives.—The control of the reactions of aluminium derivatives with **1** is more difficult than the above reported with Grignard reagents. Thus, from a practical point of view, it is more convenient to have the reaction at 25 °C, to obtain products **3** or **4**. In this case triethyl- and tributyl-aluminium, in toluene, led to compound **3** in very good yields (68–85%); but triisobutylaluminium, more sterically demanding and with a high reductive character, yielded a mixture of the alkylation–reduction compound **4** as major (52–65%), and the double reduction product **2a** as minor component

Table 4 Reaction of compound **1** with lithium derivatives

RLi	Solvent	T/°C	1/RLi	t/h	Products (% yield)
BuLi	PhMe	25	1/4	2	**5e** (60)
	Et_2O	−50	1/4	2	**5e** (26), **2e** (55)
	Et_2O	25	1/4	2	**5e** (58)
	THF	25	1/4	2	**5e** (65)
MeLi	Et_2O	−50	1/6	2	**5b** (20), **6** (50)
	Et_2O	−50	1/4	2	**6** (60)
	Et_2O	−50[a]	1/6	12	**5b** (23), **6** (65)
	THF	−50	1/6	2	**5b** (40), **6** (35)
	THF	−50	1/4	2	**6** (75)

[a] 30 min at −50 °C, and then allowed to warm to room temp.

Table 5 Reaction of compounds **1** and **10** with organocuprates

Coumarin	R_2CuLi	Solvent[a]	T[a]/°C	Products (% yield)
1	Me_2CuLi	Et_2O	−50	**10b** (90)
	Me_2CuLi	THF	−20	**10b** (65)
	Me_2CuLi[b]	Et_2O	−50	**10b** (85)
	Me_2CuLi[b]	THF	−20	**10b** (69)
	Bu_2CuLi	Et_2O	−50	**10e** (48), **2e** (15)
	Bu_2CuLi[b]	Et_2O	−50	**10e** (65)
	Bu_2CuLi[b]	THF	−50	**10e** (70)
	BuCu[b]	Et_2O	−50	**10e** (—)
10b	Me_2CuLi	Et_2O	−50	**10b** (95)
10b	Bu_2CuLi	Et_2O	−50	**10b** (90)
10e	Me_2CuLi	Et_2O	−50	**10e** (95)
10e	Me_2CuLi	Et_2O	−50	**10e** (87)

[a] The reactions were carried out in molar ratio 1/R_2CuLi, 1/3 for 2 h. [b] Boron trifluoride–diethyl ether complex was used.

(10–34%) (Table 3). The reductive character of these organometallic reagents increases in diethyl ether or THF, but their reactivity towards coumarins decreases,[1] making the reactions impossible from a synthetic point of view.

Since trimethylaluminium is less reactive than triethyl- or tributyl-aluminium, the reaction had to be carried out in refluxing toluene. However, after 3 h, only a complex mixture of products was obtained. The trimethylbenzopyran **9b**, which could not be obtained using MeMgI, could however be synthesized in moderate yield (65%) when the reaction was carried out in CH_2Cl_2.

The reaction of compound **1** with DIBAH, at room temp. yielded compound **2a**. Nevertheless, at lower temperatures (−50 °C, 2 h, **1**/DIBAH, 1/2.5), the product obtained was **11a**, which is very unstable and was isolated after purification as chromone **12a**.

Reactions with Lithium Derivatives.—Lithium derivatives react by 1,2-addition, but in our case they did not lead preferentially to the expected dialkyl derivatives **2** (Table 4). Instead, the dehydrochlorination product **5e** was obtained as major compound (25–60%) in the reactions of **1** with butyllithium.

On the other hand, methyllithium reacted with **1** to give *o*-hydroxyphenylacetylene **6** as major compound. This degradation product did not appear either in the reactions with other organometallics, or with butyllithium. Although compound **6** could be formed during the reaction, the main amount must be formed during the hydrolysis, since it diminished or disappeared when the reaction mixture was subjected to acetolysis.

Reactions with Organocuprates.—Lithium dimethyl- and dibutyl-cuprates and their boron trifluoride–diethyl ether complexes reacted with 4-chlorocoumarin **1**, giving very good yields of 4-methylcoumarin **10b** (90%) and 4-butylcoumarin **10e** (65%), respectively. Compounds **10** are stable in excess of the

reagent, and they are probably formed by copulation,[7] instead of 1,4-addition–elimination process.

Conversely, alkylcuprates which react better than lithium dialkylcuprates with α-β-unsaturated esters by a 1,4-addition process,[8] reacted with compound **1** leading to compound **10** in low yield (Table 5).

Conclusion.—4-Chlorocoumarin has been shown to be a very useful substrate in its reactions with organometallic reagents; both by its versatility in the introduction of different substituents, and by the nature of the reaction products. Provided that strict control of the reaction conditions is achieved, these otherwise cumbersome and uninteresting reactions become useful synthetic procedures.

Experimental

M.p.s were measured on a Leit Laborlux D microscope with a heating device and are uncorrected. The b.p.s correspond to the oven temperature in a kugelrohr Buchi GKR-51. NMR spectra were recorded on Bruker AC80 spectrometer and chemical shifts are given downfield from $SiMe_4$ as internal standard, *J* values are given in Hz. Mass spectra were measured on Hewlett-Packard 5988A mass spectrometer.

The starting material 4-chlorocoumarin was prepared as previously described.[9]

Reaction of Compound **1** *with Organocuprates. Synthesis of* 4-*Methyl*-1-*benzopyran*-2-*one* **10b** *and* 4-*Butyl*-1-*benzopyran*-2-*one* **10e**.—A magnetically stirred solution of organocuprate or boron trifluoride–diethyl ether complex (1.6 mmol) in the appropriate solvent (Table 5) (20 cm^3) under N_2 was cooled to −50 °C, and a solution of compound **1** (0.2 g, 1.1 mmol) in dry solvent (20 cm^3) was added dropwise. The mixture was stirred for 60 min, and quenched with saturated aq. NH_4Cl (15 cm^3). The product was extracted with Et_2O (3 × 20 cm^3), and the extract was washed sequentially with water and brine. The organic layer was chromatographed on silica gel with methylene chlorine as eluent, to yield the compounds **10b** (0.14 g, 80%) and **10e** (0.15 g, 64%). 4-*Methyl*-1-*benzopyran*-2-*one* **10b** m.p. 81–82 °C (lit.,[10] 82 °C) (Found: C, 74.8; H, 4.85. Calc. for $C_{10}H_8O_2$: C, 75.0; H, 5.0%); δ_H(80 MHz; $CDCl_3$) 2.51 (3 H, d, *J* 1), 6.18 (1 H, q, *J* 1) and 6.85–7.61 (4 H, m).

4-*Butyl*-1-*benzopyran*-2-*one* **10e** m.p. 68.5–69.5 °C (lit.,[1] 67–68 °C) (Found: C, 77.35; H, 6.8. Calc. for $C_{13}H_{14}O_2$: C, 77.2; H, 7.0%); δ_H(80 MHz; $CDCl_3$) 0.99 (3 H, td, *J* 6, 1), 1.09–1.98 (4 H, m), 2.77 (2 H, m), 6.26 (1 H, t, *J* 1) and 7.12–7.61 (4 H, m); *m/z* 202 (M^+, 20%) and 160 (100).

Reaction of Compound **1** *with Organomagnesium, Organolithium and Organoaluminium Compounds. General Procedure.*—To a magnetically stirred solution of 4-chlorocoumarin **1** (5.5 mmol) in the appropriate solvent (100 cm^3) was added dropwise (30 min) the organometallic compound under nitrogen (see Tables 1, 3 and 4). At the end of the reaction (monitored by TLC), the mixture was hydrolysed. The organic layer was decanted, dried ($MgSO_4$) and the solvent was eliminated under reduced pressure at room temp.

The conditions of hydrolysis and the methods of purification depend on the desired product, and are given below.

(*a*) 1,1-*Dialkyl*-3-*chloro*-3-(o-*hydroxyphenyl*)*prop*-2-*en*-1-*ols* **2**. The reaction was hydrolysed with saturated aqueous NH_4Cl, and the product was isolated and purified by recrystallization from Cl_4C or $CHCl_3$ from the reaction mixture.

(*b*) 1,1,3-*Trialkyl*-3-(o-*hydroxyphenyl*)*prop*-2-*en*-1-*ols* **3**. The reaction mixture was quenched with ice–water, and acidified until metallic hydroxides were just dissolved, followed by neutralization with $NaHCO_3$. The compounds were purified by recrystallization from toluene–hexane, 1/20 or by flash chromatography on silica gel with CH_2Cl_2 as eluent. It was not possible to purify compound **3e** by recrystallization, and it was transformed into 2,2,4-*trialkyl*-2H-1-*benzopyran* **9e**, when subjected to distillation.

(*c*) 1,1-*Dialkyl*-3-(o-*hydroxyphenyl*)*prop*-2-*yn*-1-*ols* **5**. The reaction mixture was hydrolysed with water at room temp. The title compounds were purified by column chromatography on silica gel, with CH_2Cl_2–Et_2O:20/1 as eluent.

(*d*) 2,2-*Dialkyl*-4-*chloro*-2H-1-*benzopyrans* **8**. The concentrate of the reaction was heated under reflux with silica gel (× 3 w/w)[11] for 1 h. The title compounds **8** were purified by column chromatography on silica gel, with hexane as eluent.

(*e*) 2,2,4-*Trialkyl*-2H-1-*benzopyrans* **9**. After concentration of the reaction mixture of 1,1,3-*trialkyl*-3-(o-*hydroxyphenyl*)*prop*-2-*en*-1-*ols* **3**, the concentrate was treated as described in (*d*).

The physical and spectral characteristics of the products, the optimized experimental conditions, and chemical yields are given below.

(E)-3-*Chloro*-3-(o-*hydroxyphenyl*)*prop*-2-*en*-1-*ol* **2a**. (DIBAH, PhMe, −50 °C, 72%) m.p. 74.5–75.5 °C (Found: C, 58.3; H, 4.75. $C_9H_9ClO_2$ requires C, 58.6; H, 4.9%); δ_H(80 MHz; $CDCl_3$) 3.95 (2 H, d, *J* 7), 6.22 (1 H, t, *J* 7) and 6.72–7.28 (4 H, m); *m/z* 168 ($M^+ + 2 - H_2O$, 17%), 166 ($M^+ - H_2O$, 55) and 165 (100).

(E)-4-*Chloro*-4-(o-*hydroxyphenyl*)-2-*methylbut*-3-*en*-2-*ol* **2b**. (MeMgI, THF, 0 °C, 75%) m.p. 106–107 °C (Found: C, 62.2; H, 6.4. $C_{11}H_{13}ClO_2$ requires C, 62.1; H, 6.2%); δ_H(80 MHz; $CDCl_3$) 1.26 (6 H, s), 6.29 (1 H, s) and 6.78–7.33 (4 H, m); *m/z* 196 ($M^+ + 2 - H_2O$, 4%), 194 ($M^+ - H_2O$, 11) and 179 (100).

(E)-1-*Chloro*-3-*ethyl*-1-(o-*hydroxyphenyl*)*pent*-1-*en*-3-*ol* **2c**. (EtMgBr, THF, 0 °C, 69%); m.p. 94–95 °C (Found: C, 64.8; H, 7.3. $C_{13}H_{17}ClO_2$ requires C, 64.9; H, 7.1%); δ_H(80 MHz; $CDCl_3$) 0.87 (6 H, t, *J* 7), 1.52 (4 H, m), 6.20 (1 H, s) and 6.78–7.25 (4 H, m); *m/z* 242 ($M^+ + 2$, <1%), 240 (M^+, 1) and 193 (100).

(E)-1-*Chloro*-1-(o-*hydroxyphenyl*)-3-*propylhex*-1-*en*-3-*ol* **2d**. (PrMgBr, THF, 0 °C, 65%) m.p. 73–74 °C (Found: C, 66.8; H, 7.75. $C_{15}H_{21}ClO_2$ requires C, 67.0; H, 7.9%); δ_H(80 MHz; $CDCl_3$) 0.85–1.05 (6 H, m), 1.19–1.52 (8 H, m), 6.12 (1 H, s) and 6.81–7.27 (4 H, m); *m/z* 252 ($M^+ + 2 - H_2O$, <1%), 250 ($M^+ - H_2O$, 2) and 207 (100).

(E)-3-*Butyl*-1-*chloro*-1-(o-*hydroxyphenyl*)*hept*-1-*en*-3-*ol* **2e**. (BuMgBr, THF, 0 °C, 76%) m.p. 77.4–78.4 °C (Found: C, 68.95; H, 8.3. $C_{17}H_{25}ClO_2$ requires C, 68.8; H, 8.5%); δ_H(80 MHz; $CDCl_3$) 1.03–1.32 (6 H, m), 1.32–1.68 (12 H, m), 6.15 (1 H, s) and 6.66–7.34 (4 H, m); *m/z* 280 ($M^+ + 2 - H_2O$, 1%), 278 ($M^+ - H_2O$, 3) and 221 (100).

(E)-1-*Chloro*-1-(o-*hydroxyphenyl*)-3-*isopropyl*-4-*methylpent*-1-*en*-3-*ol* **2f**. (Pr^iMgBr, PhMe, 25 °C, 76%) m.p. 122.3–123.3 °C (Found: C, 67.15; H, 7.85. $C_{15}H_{21}ClO_2$ requires C, 67.0; H, 7.9%); δ_H(80 MHz; $CDCl_3$) 0.90 (6 H, d, *J* 6), 0.96 (6 H, d, *J* 6), 1.85 (2 H, setp, *J* 6), 6.98 (1 H, s) and 7.00–7.31 (4 H, m); *m/z* 270 ($M^+ + 2$, >1%), 268 (M^+, 1) and 71 (100).

(Z)-3-*Ethyl*-5-(o-*hydroxyphenyl*)*hept*-4-*en*-3-*ol* **3c**. (EtMgBr, PhMe, 25 °C, 77%) m.p. 77.8–78.8 °C (Found: C, 76.7; H, 9.65. $C_{15}H_{22}O_2$ requires C, 76.9; H, 9.5%); δ_H(80 MHz; $CDCl_3$) 0.97 (9 H, m), 1.48 (4 H, q, *J* 7), 2.25 (2 H, qd, *J* 7, 1), 5.58 (1 H, t, *J* 1) and 6.79–7.21 (4 H, m); *m/z* 216 ($M^+ - H_2O$, 3%) and 187 (100).

(Z)-6-(o-*Hydroxyphenyl*)-4-*propylnon*-5-*en*-4-*ol* **3d**. (PrMgBr, Et_2O, 25 °C, 73%) b.p. 140–145 °C (2 mmHg) (the title compound decomposed to 2,2,4-*tripropyl*-2H-1-*benzopyran* **9d**); δ_H(80 MHz; $CDCl_3$) 0.97 (9 H, m), 1.05–1.72 (10 H, m), 2.20 (2 H, td, *J* 7, 1), 5.58 (1 H, t, *J* 1) and 6.83–7.18 (4 H, m); *m/z* 216 ($M^+ - H_2O$, 2%) and 215 (100).

(Z)-5-*Butyl*-7-(o-*hydroxyphenyl*)*undec*-6-*en*-5-*ol* **3e**. (Bu_3Al, PhMe, 25 °C, 79%) yellow oil (the compound decomposed to

2,2,4-*tributyl*-2H-1-*benzopyran* **9e**); δ_H(80 MHz; $CDCl_3$) 0.80–1.26 (9 H, m), 1.28–1.62 (16 H, m), 2.15–2.42 (2 H, m), 5.59 (1 H, m) and 6.76–7.14 (4 H, m); *m/z* 300 ($M^+ - H_2O$, 6%) and 243 (100).

(Z)-5-(o-*Hydroxyphenyl*)-3-*isopropyl*-2,7-*dimethylhept*-4-*en*-3-*ol* **3f**. (Pr^iMgBr, Et_2O, 25 °C, 75%) m.p. 93.6–94.6 °C (Found: C, 78.1; H, 10.4. $C_{18}H_{28}O_2$ requires C, 78.2; H, 10.2%); δ_H(80 MHz; $CDCl_3$) 0.66–0.99 (12 H, m), 0.94 (16 H, d, *J* 7), 1.83 (2 H, m), 2.39 (1 H, sept d, *J* 7, 1), 5.42 (1 H, d, *J* 1) and 6.50–7.21 (4 H, m); *m/z* 258 ($M^+ - H_2O$, 2%) and 71 (100).

(Z)-6-(o-*Hydroxyphenyl*)-2,8-*dimethylnon*-5-*en*-4-*ol* **4g**. (Bu^i_3-Al, PhMe, 25 °C, 61%) m.p. 93.6–94.6 °C (lit.,[12] 93–94 °C) (Found: C, 80.8; H, 10.2. Calc. for $C_{17}H_{26}O_2$: C, 80.9; H, 10.3%); δ_H(80 MHz; $CDCl_3$) 0.62–1.12 (12 H, m), 1.21–2.05 (4 H, m), 2.23 (2 H, m), 4.15 (1 H, dt, *J* 9, 7), 5.49 (1 H, d, *J* 9) and 6.59–7.11 (4 H, m); *m/z* 244 ($M^+ - H_2O$, 9%) and 187 (100).

4-(o-*Hydroxyphenyl*)-2-*methylbut*-3-*yn*-2-*ol* **5b**. (MeMgI, PhMe, 0 °C, 64%) m.p. 131–132 °C (Found: C, 75.1; H, 6.7. $C_{11}H_{12}O_2$ requires C, 75.0; H, 6.9%); δ_H(80 MHz; $CDCl_3$) 1.65 (6 H, s), 6.70–6.93 (2 H, m) and 7.12–7.32 (2 H, m); *m/z* 176 (M^+, 14%) and 158 (100).

3-*Ethyl*-1-(o-*hydroxyphenyl*)*pent*-1-*yn*-3-*ol* **5c**. (EtMgBr, THF, 0 °C, 67%) m.p. 72.3–73.3 °C (Found: C, 76.25; H, 7.85. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.9%); δ_H(80 MHz; $CDCl_3$) 1.08 (6 H, t, *J* 7), 1.78 (4 H, q, *J* 7) and 6.69–7.30 (4 H, m); *m/z* 204 (M^+, 7%) and 186 (100).

1-(o-*Hydroxyphenyl*)-3-*propylhex*-1-*yn*-3-*ol* **5d**. (PrMgBr, THF, 0 °C, 60%) m.p. 66–67 °C (Found: C, 77.7; H, 8.5. $C_{15}H_{20}O_2$ requires C, 77.55; H, 8.7%); δ_H(80 MHz; $CDCl_3$) 0.96 (6 H, t, *J* 7), 1.45–1.83 (8 H, m) and 6.71–7.33 (4 H, m); *m/z* 232 (M^+, 4%) and 43 (100).

3-*Butyl*-1-(o-*hydroxyphenyl*)*hept*-1-*yn*-3-*ol* **5e**. (BuMgBr, PhMe, 0 °C, 59%) m.p. 63.5–64.5 °C (Found: C, 78.6; H, 9.15. $C_{17}H_{24}O_2$ requires C, 78.4; H, 9.3%); δ_H(80 MHz; $CDCl_3$) 0.90–1.08 (6 H, m), 1.15–1.70 (12 H, m) and 6.71–7.32 (4 H, m); *m/z* 260 (M^+, 1%) and 203 (100).

1-(o-*Hydroxyphenyl*)-3-*isopropyl*-4-*methyl*-*pent*-1-*yn*-3-*ol* **5f**. (Pr^iMgBr, THF, 0 °C, 60%) m.p. 100.5–101.5 °C (Found: C, 77.65; H, 8.6. $C_{15}H_{20}O_2$ requires C, 77.55; H, 8.7%); δ_H(80 MHz; $CDCl_3$) 1.08 (6 H, d, *J* 7), 1.10 (6 H, d, *J* 7), 2.05 (2 H, sept, *J* 7) and 6.70–7.32 (4 H, m); *m/z* 232 (M^+, 1%) and 198 (100).

o-*Hydroxyphenylacetylene* **6**. (MeLi, Et_2O, −50 °C, 60%) b.p. 79–82 °C (20 mmHg) [lit.,[13] 74.5 (15 mmHg)]; δ_H(80 MHz; $CDCl_3$) 3.45 (1 H, s), 6.65–7.65 (4 H, m); *m/z* 119 (M^+ + 1, 8%) and 118 (M^+, 100).

3-*Hydroxy*-1-(o-*hydroxyphenyl*)-3-*methylbutan*-1-*one* **7b**. (MeMgI, THF, 0 °C, 60%) Hydrolysed with AcOH, purified by chromatography with PhMe as eluent; b.p. 105–110 °C (1.5 mmHg) (Found: C, 68.15; H, 7.4. $C_{11}H_{14}O_3$ requires C, 68.0; H, 7.3%); δ_H(80 MHz; $CDCl_3$) 1.36 (6 H, s), 3.16 (2 H, s) and 6.78–7.79 (4 H, m); *m/z* 194 (M^+, 5%) and 121 (100).

4-*Chloro*-2,2-*dimethyl*-2H-1-*benzopyran* **8b**. (MeMgI, THF, 0 °C, 70%) b.p. 98–100 °C (1.5 mmHg) (Found: C, 67.6; H, 5.6. $C_{11}H_{11}ClO$ requires C, 67.9; H, 5.7%); δ_H(80 MHz; $CDCl_3$) 1.44 (6 H, s), 5.71 (1 H, s) and 6.70–7.51 (4 H, m); *m/z* 196 (M^+ + 2, 3%), 194 (M^+, 10) and 170 (100).

4-*Chloro*-2,2-*diethyl*-2H-1-*benzopyran* **8c** (EtMgBr, THF, 0 °C, 65%) b.p. 100–105 °C (1.5 mmHg) (Found: C, 70.0; H, 6.6. $C_{13}H_{15}ClO$ requires C, 70.1; H, 6.8%); δ_H(80 MHz; $CDCl_3$) 0.93 (6 H, t, *J* 7), 1.56–1.86 (4 H, m), 5.62 (1 H, s) and 6.70–7.46 (4 H, m); *m/z* 224 (M^+ + 2, 1%), 222 (M^+, 3) and 193 (100).

4-*Chloro*-2,2-*dipropyl*-2H-1-*benzopyran* **8d**. (PrMgBr, THF, 0 °C, 61%) b.p. 105–110 °C (0.9 mmHg) (Found: C, 72.0; H, 7.5. $C_{15}H_{19}ClO$ requires C, 71.8; H, 7.6%); δ_H(80 MHz; $CDCl_3$) 0.80–1.31 (6 H, m), 1.37–1.79 (8 H, m), 5.64 (1 H, s) and 6.68–7.46 (4 H, m); *m/z* 196 (M^+ + 2, 5%), 194 (M^+, 15) and 207 (100).

4-*Chloro*-2,2-*dibutyl*-2H-1-*benzopyran* **8e**. (BuMgBr, THF, 0 °C, 70%) b.p. 135–139 °C (2 mmHg) (Found: C, 73.4; H, 8.5. $C_{17}H_{23}ClO$ requires C, 73.2; H, 8.3%); δ_H(80 MHz; $CDCl_3$) 0.73–1.05 (6 H, m), 1.05–1.94 (12 H, m), 5.63 (1 H, s) and 6.67–7.45 (4 H, m); *m/z* 196 (M^+ + 2, 1%), 194 (M^+, 3) and 221 (100).

2,2,4-*Trimethyl*-2H-1-*benzopyran* **9b**. (Me_3Al, Cl_2CH_2, 25 °C, 62%) b.p. 60–65 °C (1 mmHg) [lit.,[14] 63–65 °C (1 mmHg)] (Found: C, 82.55; H, 8.2. Calc. for $C_{12}H_{14}O$: C, 82.7; H, 8.0%); δ_H(80 MHz; $CDCl_3$) 1.39 (6 H, s), 1.98 (3 H, d, *J* 1), 5.39 (1 H, q, *J* 1) and 6.74–7.20 (4 H, m); *m/z* 174 (M^+, 49%) and 159 (100).

2,2,4-*Tripropyl*-2H-1-*benzopyran* **9d**. (PrMgBr, Et_2O, 25 °C, 70%) b.p. 120–125 °C (1.3 mmHg) (Found: C, 83.6; H, 9.9. $C_{18}H_{26}O$ requires C, 83.7; H, 10.1%); δ_H(80 MHz; $CDCl_3$) 0.80–1.05 (9 H, m), 1.26–1.71 (10 H, m), 2.36 (2 H, t, *J* 7), 5.26 (1 H, t, *J* 1) and 6.70–7.17 (4 H, m); *m/z* 258 (M^+, 2%) and 215 (100).

2,2,4-*Tributyl*-2H-1-*benzopyran* **9e**. (Bu_3Al, PhMe, 25 °C, 75%) b.p. 145–150 °C (1.5 mmHg) (Found: C, 83.8; H, 10.6. $C_{21}H_{32}O$ requires C, 83.95; H, 10.7%); δ_H(80 MHz; $CDCl_3$) 0.95 (9 H, m), 1.15–1.71 (16 H, m), 2.45 (2 H, t, *J* 7), 5.27 (1 H, s) and 6.63–7.19 (4 H, m); *m/z* 300 (M^+, 6%) and 243 (100).

4-*Isopropyl*-1-*benzopyran*-2-*one* **10f**. (Pr^iMgBr, Et_2O, −50 °C, 78%) b.p. 85–90 °C (0.9 mmHg) [lit.,[1] 85–90 °C (0.9 mmHg)] (Found: C, 76.75; H, 6.2. Calc. for $C_{12}H_{12}O_2$: C, 76.6; H, 6.4%); δ_H(80 MHz; $CDCl_3$) 1.31 (6 H, d, *J* 7), 3.30 (1 H, m), 6.27 (1 H, d, *J* 1) and 7.05–7.61 (4 H, m); *m/z* 188 (M^+, 51%) and 145 (100).

4-*Chloro*-2H-1-*benzopyran*-2-*ol* **11a**. (DIBAH, PhMe, −50 °C, 75%) δ_H(80 MHz; $CDCl_3$) 5.85 (1 H_A, J_{AB} 4), 5.95 (1H_B, J_{AB} 4) and 6.82–7.95 (4 H, m); this compound is unstable and during the purification it is transformed into 4*H*-1-benzopyran-4-one **12a**.[15]

(Z)-3-*Ethyl*-5-(o-*hydroxyphenyl*)*non*-4-*en*-3-*ol* **14**. Characterized as the cyclization product 4-*butyl*-2,2-*diethyl*-2H-1-*benzopyran* **15**; the reaction mixture of **2c** with BuMgBr (Table 2) was subjected to a work-up as described in the paragraph (*d*). After chromatographic separation, **15** was obtained in (68%); b.p. 140–145 °C (1.5 mmHg) (Found: C, 83.65; H, 9.7. $C_{17}H_{24}O$ requires C, 83.55; H, 9.9%); δ_H(80 MHz; $CDCl_3$) 0.75–0.94 (9 H, m), 1.61–1.22 (8 H, m), 2.33 (2 H, t, *J* 7), 5.60 (1 H, t, *J* 1) and 6.77–7.27 (4 H, m); *m/z* 244 (M^+, 3%) and 215 (100).

(Z)-5-*Butyl*-3-(o-*hydroxyphenyl*)*non*-3-*en*-5-*ol* **16**. Characterized as the cyclization product 2,2-*dibutyl*-4-*ethyl*-2H-1-*benzopyran* **17**; the reaction mixture of **2e** with EtMgBr (Table 2) was subjected to a work-up as described in the paragraph (*d*). After chromatographic separation, **17** was obtained in (63%); b.p. 145–150 °C (1.7 mmHg) (Found: C, 84.0; H, 10.5. $C_{19}H_{28}O$ requires C, 83.8; H, 10.4%); δ_H(80 MHz; $CDCl_3$) 0.86–1.98 (9 H, m), 1.20–1.61 (12 H, m), 2.27–2.54 (2 H, m), 5.26 (1 H, t, *J* 1) and 6.67–7.17 (4 H, m); *m/z* 272 (M^+,1%) and 215 (100).

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