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Reductive lithiation of cyclic benzofused ethers: a source of oxygen-functionalised organolithium compounds

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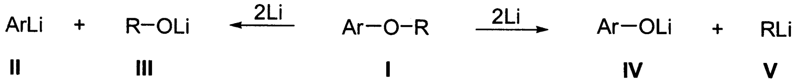
Abstract—The reaction of 2,3-dihydrobenzofuran (**1**) with lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB, 5%) in THF at 0°C for 1.5 h, followed by addition of an electrophile [E^+=H_2O, ^{t}BuCHO, $PhCH_2CHO$, $Ph(CH_2)_2CHO$, PhCHO, furfural, Me_2CO, Et_2CO, cyclopentanone, cyclohexanone, cyclooctanone, (−)-menthone] in THF at −78°C gives, after hydrolysis, compounds **3**. Some diols **3** are easily transformed into 2-substituted chromans **6** under acidic reaction conditions. The reductive lithiation of chroman (**7**) at 20°C for 3 h leads exclusively to the intermediate **8**, which is formed through a dearylation process, and isomerises to the apparently more stable benzylic intermediate **9**. The reaction of these intermediates with different electrophiles {E^+=^{t}BuCHO, PhCHO, furfural, Me_2CO, $[CH_3(CH_2)_4]_2CO$, cyclopentanone, cyclohexanone, (−)-menthone, Ph_2CO}, at −78°C in THF leads, after hydrolysis, to a mixture of regioisomers **10** and **11**. The reaction of 2,3-benzofuran (**12**) with an excess of lithium and a catalytic amount of DTBB (5%) in THF at 0°C for 45 min leads to dianionic intermediate **13** through a dealkylation process, which after hydrolysis gives 2-vinylphenol **14**. In the case of 4*H*-chromene (**15**), reductive opening is performed at 20°C for 45 min, a mixture of dearylation and dealkylation intermediates **16** and **17**, respectively, is obtained (2:1 ratio) giving, after hydrolysis, 3-phenylpropanal (**18**) and 2-allylphenol (**19**). © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Functionalised organolithium compounds[1] are of great interest in synthetic organic chemistry because by reacting with electrophiles they afford polyfunctionalised molecules in a direct manner. They have been prepared mainly by mercury–lithium transmetallation[2] with lithium metal, direct lithiation (deprotonation) of functionalised molecules with strong bases[3] and by halogen–lithium exchange with lithium metal alone[4] or in the presence of a stoichiometric[5] or catalytic[6] amount of an arene (naphthalene and DTBB being the most commonly used). The catalytic version of this procedure has shown to be more powerful than the stoichiometric one and has been used for the preparation of organolithium compounds starting from different precursors under very mild reaction conditions.[7] More recently, reductive opening of heterocycles has proved to be a direct and easy way to achieve the preparation of functionalised organolithium compounds in only one single step, starting from readily available starting materials.[8] On the other hand, phenylthioethers[9,10] are an alternative to the use of halogenated materials as precursors for organolithium compounds in good yields. However, in the case of phenylethers, this methodology is useful only for the preparation of benzyl- and allyl-lithium derivatives[11] from the corresponding benzylic and allylic ethers. Alkyl aryl ethers (**I**) have not been used extensively for the generation of organolithium compounds because of the competence of two different bond cleavages:[12] alkyl-oxygen bond cleavage (dealkylation) leading to alkyllithiums (**V**) and phenolates (**IV**) and aryl-oxygen bond cleavage (dearylation) leading to aryllithiums (**II**) and alcoholates (**III**) (Scheme 1). There are many factors which control this reductive cleavage, among them the electronic effect of the metallic cation resulting after electron transfer to the alkyl aryl ether,[13] the presence of other contraions,[14] the conformation of the substrate[13] and the polarity of the solvent.[15] Recently, we discovered that the methodology involving an arene-catalysed lithiation can also be applied to the generation of alkyllithiums from alkyl phenyl ethers.[16] Herein, we report the DTBB-catalysed lithiation of different cyclic aryl ethers for the generation of functionalised organolithium intermediates



$$\begin{array}{ccccccccc} \text{ArLi} & + & \text{R–OLi} & \xleftarrow{2\text{Li}} & \text{Ar–O–R} & \xrightarrow{2\text{Li}} & \text{Ar–OLi} & + & \text{RLi} \\ \textbf{II} & & \textbf{III} & & \textbf{I} & & \textbf{IV} & & \textbf{V} \end{array}$$

Scheme 1.

Keywords: lithiation; benzofuran; chromans; chromene.

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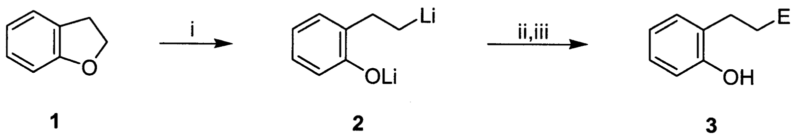


Scheme 2. *Reagents and conditions*: (i) Li, DTBB cat. (5 mol%), 0°C; (ii) $E^+=H_2O$, ^{t}BuCHO, $PhCH_2CHO$, $Ph(CH_2)_2CHO$, PhCHO, furfural, Me_2CO, Et_2CO, cyclopentanone, cyclohexanone, cyclooctanone, (−)-menthone, −78°C; (iii) $HCl–H_2O$, −78 to 20°C.

Table 1. Preparation of compounds **3**

Entry	Electrophile E^+	Product[a]			
		No.	E	Yield (%)[b]	R_f[c]
1	H_2O	**3a**	H	76 (18)	0.61 (0.53)
2	^{t}BuCHO	**3b**	^{t}BuCHOH	78 (12)	0.35 (0.18)
3	$PhCH_2CHO$	**3c**	$PhCH_2CHOH$	47 (10)	0.28 (0.07)
4	$Ph(CH_2)_2CHO$	**3d**	$Ph(CH_2)_2CHOH$	55 (7)	0.24 (0.10)
5	PhCHO	**3e**	PhCHOH	70 (15)	0.30 (0.10)
6	Furfural	**3f**	–[d]	46	0.17
7	Me_2CO	**3g**	Me_2COH	72	0.20
8	Et_2CO	**3h**	Et_2COH	69	0.28
9	Cyclopentanone	**3i**	$(CH_2)_4COH$	77	0.23
10	Cyclohexanone	**3j**	$(CH_2)_5COH$	62	0.32
11	Cyclooctanone	**3k**	$(CH_2)_7COH$	44	0.29
12	(−)-Menthone	**3l**	–[d]	33	0.63

[a] All compounds **3** were >95% pure (GLC and/or 300 MHz ^1H NMR).

[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate), based on the starting dihydrobenzofuran **1**. Isolated yield of compounds **5** is given in parenthesis.

[c] Silica gel, hexane/ethyl acetate: 3:1. R_f values of compounds **5** are given in parenthesis.

[d] See Fig. 1.

upon reductive cleavage of a carbon–oxygen bond, following the above mentioned catalytic version of the lithiation.

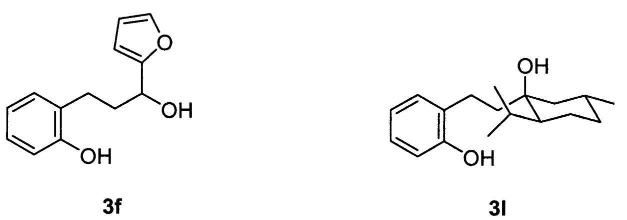
2. Results and discussion

2.1. Reductive opening of 2,3-dihydrobenzofuran (1)[17]

The reaction of commercially available 2,3-dihydrobenzofuran (**1**) with an excess of lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB; 5 mol%) in THF at 0°C for 1.5 h gave a solution of dianion **2**, which after reaction with different electrophiles [$E^+=H_2O$, ^{t}BuCHO, $PhCH_2CHO$, $Ph(CH_2)_2CHO$, PhCHO, furfural, Me_2CO, Et_2CO, cyclopentanone, cyclohexanone, cyclooctanone, (−)-menthone] at −78°C and final hydrolysis with water led to the expected products **3** (Scheme 2 and Table 1). In the case of using (−)-menthone as electrophile, compound **3l**, resulting from the attack of organolithium intermediate **2** to the less hindered down face of the carbonyl group, was obtained (Fig. 1).

In some cases, functionalised alcohols **5** were obtained as side reaction products in less than 18% yield when water and aldehydes, except for furfural, were used as electrophiles, and they were isolated and characterised (Fig. 2 and Table 1, entries 1–5 and footnotes b and c). An explanation for this result comes from the fact that two reductive cleavages in the starting 2,3-dihydrobenzofuran (**1**) can occur under these reaction conditions: the major one leads to intermediate **2** through an alkyl-oxygen bond cleavage (the so called dealkylation reaction), and the minor one, giving dianion **4** through an aryl-oxygen bond cleavage (dearylation reaction).

Diols **3** prepared as shown in Scheme 2, can act as precursors of the corresponding oxygen-containing heterocycles by a dehydration process. Thus, treatment of diols **3e**,**h**,**j**,**k** with 85% phosphoric acid under toluene reflux gave the corresponding substituted chromans **6e**,**h**,**j**,**k** (Scheme 3 and Table 2). In the case of benzylic or tertiary diols, yields

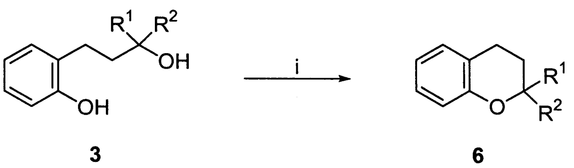


3f **3l**

Figure 1.

4 **5**

Figure 2.



Scheme 3. *Reagents and conditions*: (i) H_3PO_4, PhMe, 110°C.

Table 2. Cyclization of compounds **3**. Preparation of compounds **6**

Entry	Starting diol	Product[a]				
		No.	R^1	R^2	Yield (%)[b]	R_f[c]
1	**3e**	**6e**	Ph	H	>95	0.20
2	**3h**	**6h**	Et	Et	92	0.28
3	**3j**	**6j**	$(CH_2)_5$		>95	0.29
4	**3k**	**6k**	$(CH_2)_7$		68	0.23

[a] All compounds **6** were >95% pure (GLC and/or 300 MHz ^1H NMR).

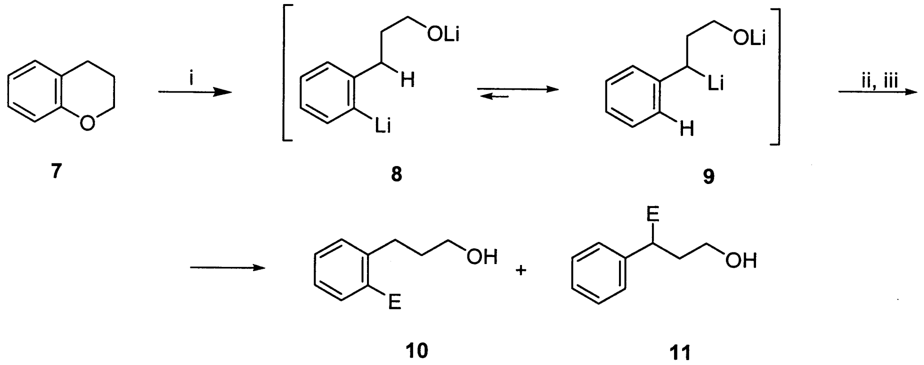
[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate), based on the starting diol **3**.

[c] Silica gel, hexane.

were almost quantitative. For other diols of type **3**, a variable amount of olefination and rearrangement products took place during acidic cyclization.

2.2. Reductive opening of chroman (7)

In order to continue our study on reductive opening of cyclic phenyl ethers, chroman (**7**),[18] [homologous heterocycle of 2,3-dihydrobenzofuran (**1**)] was prepared starting from commercially available dihydrocumarin in a two-step process in 70% overall yield: (a) reduction with lithium aluminium hydride to the corresponding diol and (b) acidic cyclization. The reaction of chroman (**7**) with an excess of lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB; 5 mol%) in THF at temperatures ranging from 0 to 20°C for 3 h gave, after reaction with water as electrophile, 3-phenyl-1-propanol (**10a**, Scheme 4 and Table 3, entry 1). Reaction time for the total consumption of chroman (**7**) is longer than in the case of 2,3-dihydrofuran (**1**), and it was necessary to perform the reaction at higher temperature, 20°C instead of 0°C. Just to ensure the presence of the arene catalyst along the whole lithiation process, 0.04 mL of a 1.0 M THF solution of DTBB was added every 30 min. However, the main difference being that the reductive opening of chroman (**7**) takes place exclusively through aryl-oxygen bond cleavage (dearylation) to give intermediate **8**, whereas in the case of 2,3-dihydrobenzofuran (**1**), dealkylation is the major process as it was commented above. When different carbonyl compounds were used as electrophiles {E^+=^{t}BuCHO, PhCHO, furfural, Me_2CO, $[CH_3(CH_2)_4]_2CO$, Ph_2CO, cyclopentanone, cyclohexanone, (−)-menthone}, a mixture of regioisomeric compounds **10**



Scheme 4. *Reagents and conditions*: (i) Li, DTBB cat. (5 mol%), 0 to 25°C; (ii) E^+=H_2O, ^{t}BuCHO, PhCHO, furfural, Me_2CO, $[CH_3(CH_2)_4]_2CO$, cyclohexanone, (−)-menthone, Ph_2CO, −78°C; (iii) H_3O^+, −78 to 20°C.

Table 3. Reductive opening of chroman **7** and reaction with electrophiles. Isolation of compounds **10** and **11**

Entry	Electrophile E^+	Product[a]			
		No.	E	Yield (%)[b]	R_f[c]
1	H_2O	**10a**	H	95	0.88
2	^{t}BuCHO	**10b**	^{t}BuCHOH	10	0.41
3		**11b**	^{t}BuCHOH	(35+7)[d]	(0.41, 0.48)[e]
4	PhCHO	**11c**	PhCHOH	34	0.31
5	Furfural	**11d**	–[f]	(16+15)[d]	(0.35, 0.31)[e]
6	Me_2CO	**10e**	Me_2COH	9	0.28
7		**11e**	Me_2COH	23	0.18
8	$[CH_3(CH_2)_4]_2CO$	**11f**	$[CH_3(CH_2)_4]_2COH$	49	0.68
9	Ph_2CO	**11g**	Ph_2COH	52	0.53
10	Cyclopentanone	**10h**	$(CH_2)_4COH$	3	0.33
11		**11h**	$(CH_2)_4COH$	27	0.25
12	Cyclohexanone	**11i**	$(CH_2)_5COH$	27	0.30
13	(−)-Menthone	**11j**	–[f]	(39+4)[d]	(0.52, 0.49)[e]

[a] All compounds **10** and **11** were >92% pure (GLC and/or 300 MHz ^1H NMR).

[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate), based on the starting dihydrobenzopyran **7**.

[c] Silica gel, hexane/ethyl acetate: 1:1.

[d] Isolated as a diastereomeric mixture and separated by column chromatography.

[e] R_f values of each diastereomer, respectively.

[f] See Fig. 3.

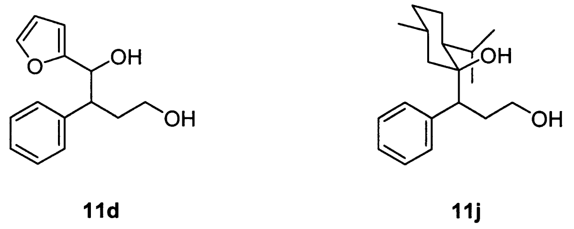


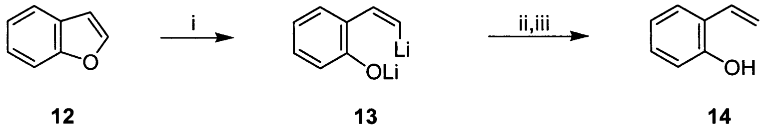
Figure 3.

and **11** were surprisingly obtained. These results indicate that dianions **8** and **9** were involved as reaction intermediates in the process. A possible explanation for this is that after reductive opening of the starting heterocycle to give intermediate **8**, and due to the reaction conditions assayed (room temperature and long reaction time), the initially formed dianion **8** is in equilibrium with the apparently more stable benzylic dianion **9** through an inter- or intramolecular acid–base process. Minor compounds **10** could not be isolated in all cases, which means that the intermediate dianion **9** predominates in the equilibrium. All attempts to adjust the reaction conditions for the preparation of only one of the intermediates failed: shorter reaction times led to a partial conversion of the starting material **7** and longer reaction times led to decomposition of dianionic intermediates **8** and **9** by proton abstraction and, consequently, to lower yields by reacting with electrophiles. The reaction of the oxygen-functionalised organolithium compound **9** with prostereogenic carbonyl compounds, such as pivaldehyde, furfural and (−)-menthone, led to a mixture of diastereomeric diols **11** (Table 3, entries 3, 5 and 13), which were separated chromatographically and characterised. As it was previously commented, when (−)-menthone was used as electrophile, compound **11j**, resulting from the attack of organolithium intermediate **9** to the less hindered down face of the carbonyl group, was obtained (Fig. 3).

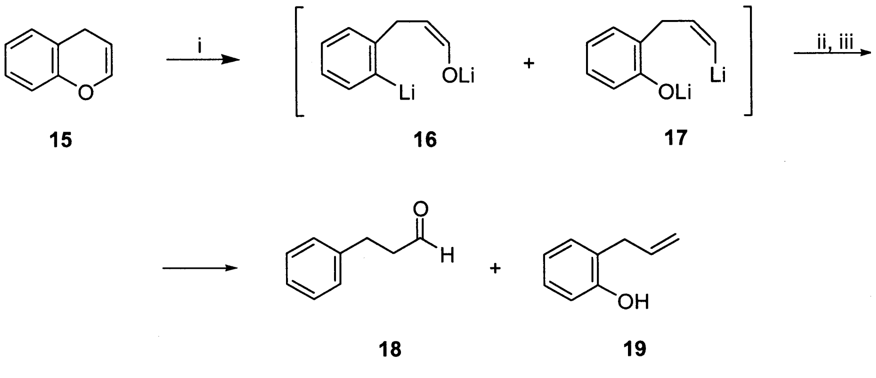
2.3. Reductive opening of 2,3-benzofuran (12)[19] and 4*H*-chromene (15)

Finally, we studied the reductive opening of other cyclic phenyl ethers, such as 2,3-benzofuran (**12**) and 4*H*-chromene (**15**), which differ from 2,3-dihydrobenzofuran (**1**) and chroman (**7**) in the hybridisation of the carbon atom bonded to oxygen at the heterocyclic ring. We recently reported that the reaction of 2,3-benzofuran (**12**) with an excess of lithium powder and a catalytic amount of DTBB (5 mol%) in THF at 0°C for 45 min led, after hydrolysis with water, to 2-vinylphenyl (**14**) in 93% isolated yield, dilithiated compound **13** being involved as reaction intermediate in this process (Scheme 5). In this case, a dealkylation process takes place exclusively, the *Z*-configuration of the double bond in **13** being proved by reaction with other electrophiles.[19]

4*H*-Chromene (**15**)[20] was prepared from dihydrocumarine by successive reduction with lithium tri-(*tert*-butoxy)aluminohydride to the corresponding hemiacetal, followed by *in situ* acylation and final pyrolytic elimination, in almost 70% overall yield. When 4*H*-chromene (**15**) was submitted to the same lithiation reagent as above, at 20°C for 45 min, followed by hydrolysis with water, a mixture of 3-phenylpropanal (**18**) and 2-allylphenol (**19**) in a 2:1 ratio, was respectively obtained in 95% overall yield, intermediates **16** and **17** being probably involved in the reaction. In this case, dearylation is predominant over dealkylation. When different carbonyl compounds were used as electrophiles, a complex mixture of reaction products was obtained, due in part to the presence of two reactive positions in enolate intermediate **16**. Therefore, this approach is not synthetically useful (Scheme 6).



Scheme 5. *Reagents and conditions*: (i) Li, DTBB cat. (5 mol%), 0°C; (ii) H_2O, −78°C; (iii) H_3O^+, −78 to 20°C.



Scheme 6. *Reagents and conditions*: (i) Li, DTBB cat. (5 mol%), 0 to 25°C; (ii) H_2O, −78°C; (iii) H_3O^+, −78 to 20°C.

3. Conclusions

We report here on the reductive opening of different cyclic alkyl aryl ethers. In the case of 2,3-dihydrobenzofuran (**1**), reductive lithiation led mainly to the dealkylation product **2**, which by reaction with carbonyl compounds gave diols of type **3**. 2-Substituted chromans (**6**) can be easily prepared by acidic dehydration of diols **3**. Reductive opening of chroman (**7**) led exclusively to the dearylation intermediate **8**, which isomerised to the more stable benzylic dianion **9**. Reductive opening of 2,3-benzofuran (**12**) gave only the product of dealkylation **13**, meanwhile 4*H*-chromene (**15**) led to a 2:1 mixture of intermediates **16** and **17**, which are formed through dearylation and dealkylation processes, respectively. We can conclude after these experimental results that the ring size plays an important role in the regioselectivity of the reductive opening of these systems. In the case of five-membered rings, dealkylation is favoured over dearylation, however, for six-membered cyclic aryl alkyl ethers, dearylation occurs predominantly. The hybridisation of the carbon atom bonded to the oxygen, which does not belong to the aromatic ring, is also important in the regioselectivity of the ring opening. Dealkylation is favoured over dearylation as the s character of the hybridisation of the mentioned carbon atom increases. In summary, stereoelectronic factors control the regiochemistry of all these processes, the ring size being important for the reaction conditions needed for the reductive opening to take place, (0°C in the case of five-membered rings and 20°C for six-membered rings). From the above-mentioned considerations, we conclude that the reported reductive cleavage reactions seem to be very sensitive to small changes in electronic distribution.

4. Experimental

4.1. General

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware. All reagents were commercially available and were used as received. THF was distilled from sodium benzophenone ketyl. Melting points were recorded in a Reichert Thermovar and are uncorrected. IR spectra were measured (neat) with a Nicolet Impact 400 D-FT Spectrometer. NMR spectra were recorded with a Bruker AC-300 using $CDCl_3$ as the solvent. LRMS and HRMS were measured with Shimadzu GC/HS QP-5000 and Finingan MAT95 S spectrometers, respectively. The purity of volatile products and the chromatographic analyses (GLC) were determined with a Hewlett–Packard HP-5890 instrument equipped with a flame ionisation detector and a 12 m capillary column (0.2 mm diam., 0.33 μm film thickness), using nitrogen (2 mL/min) as carrier gas, $T_{injector}$=275°C, $T_{detector}$=300°C, T_{column}=80°C (3 min) and 80–270°C (15°C/min), P=40 kPa. Elemental analyses were performed by the Mycroanalyses Service at the University of Alicante.

4.2. Reductive lithiation of 2,3-benzofuran (1) and reaction with electrophiles

*Isolation of compounds **3** and **5**: general procedure*. To a blue suspension of lithium powder (140 mg, 20 mmol) and a catalytic amount of DTBB (50 mg, 0.19 mmol; 5% molar) in THF (4 mL) was added 2,3-dihydrobenzofuran (**1**, 240 mg, 0.23 mL, 2.0 mmol) at 0°C and the resulting mixture was stirred for 1.5 h at the same temperature. Then, it was cooled down at −78°C and the corresponding electrophile (2.4 mmol, 0.5 mL in the case of H_2O) was added and after 15 min it was hydrolysed with 3N hydrochloric acid. The reaction mixture was allowed to reach the ambient temperature and it was extracted with ethyl acetate (3×20 mL), the organic layer dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure products **3** and **5**. Compounds **3a** and **5a** were characterised by comparison of their spectroscopic data with those reported in the literature.[21] Yields and R_f values are given in Table 1, physical, analytical and spectroscopic data follow.

4.2.1. 1-(2-Hydroxyphenyl)-4,4-dimethyl-3-pentanol (3b). Colourless liquid; ν (film) 3345 (OH), 1264, 1244 cm^{-1} (C–O); δ_H 0.87 (9H, s, $3CH_3$), 1.60–1.87 (2H, m, CH_2), 2.50 (2H, br s, 2OH), 2.69–2.86 (2H, m, CH_2), 3.19–3.23 (1H, m, C*H*OH), 6.82–7.24 (4H, m, ArH); δ_C 25.6 (CH_3), 26.5 [$C(CH_3)_3$], 31.5 (CH_2), 34.7 (CH_2), 78.7 (COH), 116.3, 120.5, 127.5, 127.7, 130.4, 154.6 (ArC); *m/z* 208 (M^+, 14%), 147 (63), 107 (100); HRMS: M^+, found 208.1469. $C_{13}H_{20}O_2$ requires 208.1463.

4.2.2. 4-(2-Hydroxyphenyl)-1-phenyl-2-butanol (3c). Colourless liquid; ν (film) 3329 (OH), 1265, 1243 cm^{-1} (C–O); δ_H 1.71–1.86 (2H, m, $ArCH_2CH_2$), 2.36 (2H, br s, 2OH), 2.60–2.85 (4H, m, $ArCH_2$, $PhCH_2$), 3.71–3.89 (1H, m, C*H*OH), 6.75–7.26 (9H, m, ArH); δ_C 25.7 ($ArCH_2$), 36.9 ($ArCH_2CH_2$), 43.8 ($PhCH_2$), 71.4 (COH), 116.1, 120.5, 126.5, 127.4, 128.5, 129.3, 130.4, 130.45, 137.9, 154.4 (ArC); *m/z* 242 (M^+,14%), 150 (63), 133 (64), 107 (100), 91 (64); HRMS: M^+, found 242.1302. $C_{16}H_{18}O_2$ requires 242.1307.

4.2.3. 1-(2-Hydroxyphenyl)-5-phenyl-3-pentanol (3d). White solid, mp 87–88°C (pentane/dichloromethane); [Found: C, 78.99; H, 7.84. $C_{17}H_{20}O_2$ requires C, 79.04; H, 7.87]; ν (KBr) 3311 (OH), 1241 cm^{-1} (C–O); δ_H 1.70–1.79 (4H, m, $ArCH_2$, $PhCH_2$), 2.52–2.88 (4H, m, CH_2COHCH_2), 3.18 (2H, br s, 2OH), 3.54–3.65 (1H, m, C*H*OH), 6.80–7.24 (9H, m, ArH); δ_C 25.6 ($ArCH_2$), 32.0 ($PhCH_2$), 37.4, 39.1 (CH_2COHCH_2), 70.4 (COH), 116.0, 120.7, 125.8, 127.4, 128.2, 128.3, 130.5, 141.8, 154.2 (ArC); *m/z* 256 (M^+, 12%), 238 (39), 147 (55), 107 (100), 91 (88); HRMS: M^+, found 242.1302. $C_{16}H_{18}O_2$ requires 242.1307.

4.2.4. 3-(2-Hydroxyphenyl)-1-phenyl-1-propanol (3e). Colourless oil; ν (film) 3327 (OH), 1243 cm^{-1} (C–O); δ_H 1.84–2.08 (2H, m, $ArCH_2CH_2$), 2.63–2.90 (2H, m, $ArCH_2$), 3.82 (2H, br s, 2OH), 4.54 (1H, dd, J=9.8, 3.7 Hz, C*H*OH), 6.76–6.86, 7.03–7.26 (9H, 2m, ArH); δ_C 26.0 ($ArCH_2$), 39.3 ($ArCH_2CH_2$), 73.0 (COH), 116.1, 120.7, 125.7, 127.4, 127.5, 127.6, 128.4, 130.5, 143.8, 154.2 (ArC); *m/z* 228 (M^+, 2%), 210 (100), 104 (55), 91 (55), 77 (64); HRMS: M^+, found 228.1140. $C_{15}H_{16}O_2$ requires 228.1150.

4.2.5. 1-Furyl-3-(2-hydroxyphenyl)-1-propanol (3f). Colourless oil; ν (film) 3370 (OH), 1265, 1242 cm^{-1}

(C–O); δ_H 2.00–2.30 (2H, m, ArCH$_2$), 2.67–2.92 (2H, m, ArCH$_2$C*H*$_2$), 2.44 (2H, br s, 2OH), 4.60 (1H, dd, *J*=9.7, 4.0 Hz, C*H*OH), 6.19 (1H, d, *J*=3.7 Hz, HC═CO), 6.26–6.29 (1H, m, *H*C═CHO), 6.79–7.11 (5H, ArH, HC═C*H*O); δ_C 25.5 (ArCH$_2$), 35.3 (ArCH$_2$*C*H$_2$), 71.1 (COH), 106.1, 110.1, 116.0, 120.7, 127.1, 127.5, 130.5, 142.0, 154.2, 155.9 (ArC, OC═CHCH═CHO); *m/z* 200 (M$^+$−H$_2$O, 90%), 94 (100); HRMS: M$^+$−H$_2$O, found 200.0840. $C_{13}H_{12}O_2$ requires 200.0837.

4.2.6. 4-(2-Hydroxyphenyl)-2-methyl-2-butanol (3g). Colourless liquid; ν (film) 3380 (OH); 3091, 3014 cm^{-1} (ArH); δ_H 1.29 (6H, s, 2CH$_3$), 1.77–1.82, 2.69–2.75 (4H, 2m, ArCH$_2$CH$_2$), 3.10 (2H, br s, 2OH), 6.80–7.12 (4H, m, ArH); δ_C 24.7 (ArCH$_2$), 29.4 [CH(*C*H$_3$)$_2$], 43.2 (ArCH$_2$*C*H$_2$), 71.8 (COH), 116.1, 120.3, 127.3, 128.8, 130.0, 154.0 ArC); *m/z* 180 (M$^+$, 3%), 107 (100); HRMS: M$^+$, found 180.1160. $C_{11}H_{16}O_2$ requires 180.1150.

4.2.7. 3-Ethyl-1-(2-hydroxyphenyl)-3-pentanol (3h). Colourless liquid; ν (film) 3353 (OH), 1241 cm^{-1} (C–O); δ_H 0.87 (6H, t, *J*=7.7 Hz, 2CH$_3$), 1.54 [4H, q, *J*=7.7 Hz, (C*H*$_2$CH$_3$)$_2$], 1.70–1.76 (2H, m, ArCH$_2$C*H*$_2$), 2.65 (2H, t, *J*=7.9 Hz, ArCH$_2$), 2.95 (2H, br s, 2OH), 6.79–6.84, 7.04–7.29 (4H, 2m, ArH); δ_C 7.9 (CH$_3$), 24.0 (ArCH$_2$), 30.6 [(*C*H$_2$)$_2$COH], 38.1 (ArCH$_2$*C*H$_2$), 75.9 (COH), 116.1, 120.2, 127.3, 129.0, 130.0, 154.0 (ArC); *m/z* 208 (M$^+$, 1%), 161 (61), 107 (100); HRMS: M$^+$, found 208.1482. $C_{13}H_{20}O_2$ requires 208.1463.

4.2.8. 1-[2-(2-Hydroxyphenyl)ethyl]cyclopentanol (3i). White solid, mp 106–107°C (pentane/dichloromethane); [Found: C, 75.43; H, 8.83. $C_{13}H_{18}O_2$ requires C, 75.68; H, 8.80]; ν (KBr) 3394 (OH); 1245 cm^{-1} (C–O); δ_H 1.51–1.92 (10H, m, 5CH$_2$), 2.75 (2H, t, *J*=7.6 Hz, ArCH$_2$), 3.12 (2H, br s, 2OH), 6.79–7.09 (4H, m, ArH); δ_C 23.7, 25.4, 39.7, 41.4 (CH$_2$), 83.1 (COH), 116.1, 120.4, 127.2, 129.0, 130.1, 154.0 (ArC); *m/z* 206 (M$^+$, 0.5%), 107 (100); HRMS: M$^+$, found 206.1322. $C_{13}H_{18}O_2$ requires 206.1307.

4.2.9. 1-[2-(2-Hydroxyphenyl)ethyl]cyclohexanol (3j). Colourless oil; ν (film) 3381 (OH), 1243 cm^{-1} (C–O); δ_H 1.49–1.60 (10H, m, 5CH$_2$), 1.78 (2H, t, *J*=7.6 Hz, ArCH$_2$C*H*$_2$), 2.23 (2H, br s, 2OH), 2.70 (2H, t, *J*=7.6 Hz, ArCH$_2$), 6.79–6.85, 7.06–7.10 (4H, 2m, ArH); δ_C 22.4, 23.7, 25.6, 37.5, 41.4 (CH$_2$), 72.6 (COH), 116.2, 120.2, 127.3, 129.1, 130.0, 154.1 (ArC); *m/z* 220 (M$^+$, 2%), 107 (100); HRMS: M$^+$, found 220.1467. $C_{14}H_{20}O_2$ requires 220.1463.

4.2.10. 1-[2-(2-Hydroxyphenyl)ethyl]cyclooctanol (3k). Colourless oil; ν (film) 3528, 3272 (OH), 1265, 1231 cm^{-1} (C–O); δ_H 1.41–1.95 (16H, m, 7CH$_2$), 2.68–2.73 (2H, m, ArCH$_2$C*H*$_2$), 3.12 (1H, s, OH), 3.38 (1H, s, OH), 6.69–7.08 (4H, m, ArH); δ_C 22.8, 24.4, 25.4, 28.7, 36.4, 42.2 (CH$_2$), 74.3 (COH), 115.5, 119.9, 127.0, 130.1, 130.3, 155.5 (ArC); *m/z* 248 (M$^+$, 1%), 107 (100), 81 (59); HRMS: M$^+$, found 248.1767. $C_{16}H_{24}O_2$ requires 248.1776.

4.2.11. (1*S*,2*S*,5*R*)-1-[2-(2-Hydroxyphenyl)ethyl]-2-isopropyl-5-methylcyclohexanol (3l). Colourless oil; ν (film) 3214 (OH), 3061, 3093, 3036 (ArH), 1233 cm^{-1} (C–O); δ_H 0.86–0.92 (9H, m, 3CH$_3$), 1.00–2.18 (11H, m, 4CH$_2$, 3CH), 2.51–2.78 (4H, m, ArCH$_2$, 2OH), 6.79–7.09 (4H, m, ArH); δ_C 18.0 (CH$_3$), 20.7 (CH$_2$), 22.4, 23.6 (CH$_3$), 24.4 (CH$_2$), 25.4, 28.1 (CH), 34.9, 40.4, 45.9 (CH$_2$), 49.1 (CH), 75.0 (COH); 115.9, 120.2, 127.3, 129.0, 129.9, 154.0 (ArC); *m/z* 276 (M$^+$, 1%), 107 (100), 95 (65); HRMS: M$^+$, found 276.2083. $C_{18}H_{28}O_2$ requires 276.2089.

4.2.12. 1-[2-(2-Hydroxyethyl)phenyl]-2,2-dimethyl-1-propanol (5b). Colourless liquid; ν (film) 3381 (OH); 3053, 3026 (ArH); 1240 cm^{-1} (C–O); δ_H 0.93 (9H, s, 3CH$_3$), 2.03 (2H, br s, 2OH), 2.75–2.84 (1H, m, ArC*H*H), 3.02–3.12 (1H, m, ArCH*H*), 3.71–3.76 (2H, t, *J*=6.4 Hz, C*H*$_2$OH), 4.77 (1H, s, C*H*OH), 7.10–7.44 (4H, m, ArH); δ_C 26.2 (CH$_3$), 35.8 (ArCH$_2$), 36.7 [*C*(CH$_3$)$_3$], 63.8 (CH$_2$OH), 77.4 (CHOH), 125.9, 127.2, 128.3, 129.6, 136.6, 140.9 (ArC); *m/z* 190 (M$^+$−H$_2$O, 1%), 133 (100); HRMS: M$^+$, found 208.1469. $C_{13}H_{20}O_2$ requires 208.1463.

4.2.13. 1-[2-(2-Hydroxyethyl)phenyl]-2-phenylethanol (5c). Colourless oil; ν (film) 3344 (OH), 3085, 3060, 3026 (ArH), 1264 cm^{-1} (C–O); δ_H 2.69–3.08 (6H, m, ArCH$_2$, PhCH$_2$, 2OH), 3.71–3.81 (2H, m, ArCH$_2$C*H*$_2$), 5.14 (2H, t, *J*=6.7 Hz, ArCH), 7.15–7.31 (9H, m, ArH); δ_C 35.0, 44.6 (CH$_2$), 63.6 (CH$_2$OH), 71.4 (CHOH), 126.3, 126.6, 126.9, 127.8, 128.5, 129.4, 130.0, 136.1, 138.4, 142.0 (ArC); *m/z* 224 (M$^+$−H$_2$O, 0.5%), 133 (100); HRMS: M$^+$−H$_2$O, found 224.1211. $C_{16}H_{16}O$ requires 224.1201.

4.2.14. 1-[2-(2-Hydroxyethyl)phenyl]-3-phenyl-1-propanol (5d). Colourless oil; ν (film) 3381 (OH), 3085, 3063, 3027 (ArH), 1276 cm^{-1} (C–O); δ_H 1.96–2.25 (2H, m, C*H*$_2$CHOH), 2.57–2.91 (6H, m, ArCH$_2$, PhCH$_2$, 2OH), 3.62–3.81 (2H, m, C*H*$_2$OH), 4.88 (1H, dd, *J*=8.3, 5.2 Hz, C*H*OH), 7.07–7.44 (9H, m, ArH); δ_C 32.5, 34.8, 38.8 (CH$_2$), 63.5 (CH$_2$OH), 69.2 (CHOH), 125.8, 125.9, 126.9, 128.3, 128.4, 128.5, 130.2, 136.5, 141.8, 142.5 (ArC); *m/z* 256 (M$^+$, 0.5%), 133 (100); HRMS: M$^+$, found 256.1459. $C_{17}H_{20}O_2$ requires 256.1463.

4.2.15. 2-[2-(Hydroxyphenylmethyl)phenyl]ethanol (5e). Colourless oil; ν (film) 3344 (OH), 1265 cm^{-1} (C–O); δ_H 2.77–3.05 (4H, m, ArCH$_2$, 2OH), 3.70–3.83 (2H, m, ArCH$_2$C*H*$_2$), 6.03 (1H, d, *J*=3.7 Hz, C*H*OH), 7.17–7.33 (9H, m, ArH); δ_C 34.9 (ArCH$_2$), 63.5 (ArCH$_2$*C*H$_2$), 72.7 (CHOH), 126.6, 126.7, 127.1, 128.0, 128.2, 128.3, 130.2, 137.3, 142.3, 143.2 (ArC); *m/z* 228 (M$^+$, 1.5%), 210 (100), 104 (60), 91 (63), 79 (60), 77 (89); HRMS: M$^+$, found 228.1155. $C_{15}H_{16}O_2$ requires 228.1150.

4.3. Acydic cyclization of diols 3

*Isolation of compounds **6**: general procedure*. To a solution of the corresponding diol **3e**,**h**,**j**,**k** (0.5 mmol) in toluene (3 mL) was added 85% phosphoric acid (0.2 mL). The reaction mixture was heated at 110°C for 4 h, then toluene was removed by distillation and the resulting residue was hydrolysed with water and extracted with ethyl acetate (3×15 mL), the organic layer dried over Na$_2$SO$_4$ and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel; hexane) to yield pure products **6e**,**h**,**j**,**k**. Compound **6e** was characterised by comparison of its spectroscopic data with those reported in the literature.[22] Yields and R_f values are given in Table 2, physical, analytical and spectroscopic data follow.

4.3.1. 2,2-Diethylchroman (6h). Colourless liquid; ν (film) 3063, 3037, 3020 (ArH), 1247 cm^{-1} (C–O); δ_H 0.84 (6H, t, J=7.6 Hz, 2CH$_3$), 1.19 (2H, t, J=6.7 Hz, ArCH$_2$C*H*$_2$), 1.44–1.75 (4H, m, 2CH$_2$), 2.66 (2H, t, J=6.7 Hz, ArCH$_2$), 6.70–6.75, 6.95–7.02 (4H, 2m, ArH); δ_C 7.5 (CH$_3$), 21.8, 27.9, 28.3 (CH$_2$), 78.3 (CO), 117.3, 119.4, 121.5, 127.2, 129.3, 154.1 (ArC); *m/z* 190 (M$^+$, 16%), 161 (60), 107 (100); HRMS: M$^+$, found 190.1355. $C_{13}H_{18}O$ requires 190.1358.

4.3.2. Spiro[cyclohexane-1,2′-chroman] (6j). Colourless oil; ν (film) 3080 (ArH), 1243 cm^{-1} (C–O); δ_H 1.26–1.81 (12H, m, 6CH$_2$), 2.75 (2H, t, J=6.7 Hz, ArCH$_2$), 6.78–6.83, 7.02–7.26 (4H, 2m, ArH); δ_C 21.6, 21.8, 26.0, 31.5, 35.2 (CH$_2$), 74.6 (CO), 117.3, 119.5, 121.6, 127.1, 129.4, 153.8 (ArC); *m/z* 202 (M$^+$, 30%), 107 (100); HRMS: M$^+$, found 202.1364. $C_{14}H_{18}O$ requires 202.1358.

4.3.3. Spiro[cyclooctane-1,2′-chroman] (6k). Colourless oil; ν (film) 3063, 3037, 3019 (ArH), 1254, 1228 cm^{-1} (C–O); δ_H 1.44–1.84 (14H, m, 7CH$_2$), 1.96–2.05 (2H, m, CH$_2$), 2.72 (2H, t, J=7.0 Hz, ArCH$_2$), 6.75–6.81, 7.02–7.09 (4H, 2m, ArH); δ_C 21.8, 22.0, 25.2, 28.3, 30.7, 30.9, 33.5 (CH$_2$), 78.5 (CO), 117.4, 119.4, 121.4, 127.2, 129.3, 153.8 (ArC); *m/z* 230 (M$^+$, 12%), 107 (100); HRMS: M$^+$, found 230.1674. $C_{16}H_{22}O$ requires 230.1671.

4.4. Reductive opening of chroman (7) and reaction with electrophiles

Isolation of compounds ***10*** *and* ***11****: general procedure*. To a blue suspension of lithium powder (140 mg, 20 mmol) and a catalytic amount of DTBB (50 mg, 0.19 mmol; 5% molar) in THF (4 mL) was added chroman (**7**, 260 mg, 0.26 mL, 2.0 mmol) at 0°C and the resulting mixture was allowed to reach 20°C. The reaction mixture was stirred for 3 h at the same temperature, but every 30 min, 0.04 mL of a 1.0 M THF solution of DTBB (54 mg, 0.2 mmol in 0.2 mL of THF) was added. Then, it was cooled down at −78°C and the corresponding electrophile (2.4 mmol, 0.5 mL in the case of H_2O) was added and after 15 min it was hydrolysed with 3N hydrochloric acid. The reaction mixture was allowed to reach the ambient temperature and it was extracted with ethyl acetate (3×20 mL), the organic layer dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure products **10** and **11**. Compound **10a** was characterised by comparison of its spectroscopic data with those described in the literature.[21] Yields and R_f values are given in Table 3, physical, analytical and spectroscopic data follow.

4.4.1. 1-[2-(3-Hydroxypropyl)phenyl]-2,2-dimethyl-1-propanol (10b). Colourless liquid; ν (film) 3384 (OH), 3083, 3057, 3027 (ArH), 1265 cm^{-1} (C–O); δ_H 0.96 (9H, s, 3CH$_3$), 1.83–2.26 (4H, m, ArCH$_2$CH$_2$), 2.86 (2H, br s, 2OH), 3.63 (2H, t, J=6.1 Hz, C*H*$_2$OH), 4.82 (1H, s, C*H*OH), 7.16–7.28 (4H, m, ArH); δ_C 26.2 (CH$_3$), 28.9 (ArCH$_2$), 34.9 (ArCH$_2$*C*H$_2$), 36.7 [*C*(CH$_3$)$_3$], 61.9 (CH$_2$OH), 80.3 (COH), 125.5, 127.1, 127.9, 128.0, 129.0, 139.7 (ArC); *m/z* 222 (M$^+$, 0.5%), 147 (100), 129 (68); HRMS: M$^+$−H$_2$O–^{t}Bu, found 147.0837. $C_{10}H_{11}O$ requires 147.0810.

4.4.2. 2-[2-(3-Hydroxypropyl)phenyl]-2-propanol (10e). Colourless liquid; ν (film) 3403 (OH), 3055 (ArH), 1265 cm^{-1} (C–O); δ_H 1.68 (6H, s, 2CH$_3$), 1.92–1.97 (2H, m, CH$_2$), 2.68 (2H, br s, 2OH), 3.11 (2H, t, J=7.4 Hz, ArCH$_2$), 3.63 (2H, t, J=5.9 Hz, C*H*$_2$OH), 7.11–7.37 (4H, m, ArH); δ_C 29.3 (CH$_2$), 32.0 (CH$_3$), 35.0 (CH$_2$), 61.7 (CH$_2$OH), 74.1 (COH), 125.5, 125.5, 127.2, 131.4, 140.3, 145.1 (ArC); *m/z* 179 (M$^+$−CH$_3$, 8%), 176 (M$^+$−H$_2$O, 10%), 143 (60), 43 (100); HRMS: M$^+$−CH$_3$, found 179.1061. $C_{11}H_{15}O_2$ requires 179.1072.

4.4.3. 1-[2-(3-Hydroxypropyl)phenyl]cyclopentanol (10h). Colourless oil; ν (film) 3403 (OH), 3055 (ArH), 1266 cm^{-1} (C–O); δ_H 1.50–1.64 (4H, m, CH$_2$, 2OH), 1.71–1.82 (2H, m, CH$_2$), 1.89–2.00 (2H, m, CH$_2$), 2.07–2.21 (4H, m, 2CH$_2$), 3.06 (2H, t, J=7.5 Hz, ArCH$_2$), 3.61 (2H, t, J=5.9 Hz, C*H*$_2$OH), 7.10–7.41 (4H, m, ArH); δ_C 23.5, 28.9, 34.7, 40.7 (CH$_2$), 61.5 (CH$_2$OH), 84.3 (COH), 125.4, 125.5, 127.4, 131.0, 141.3, 143.7 (ArC); *m/z* 220 (M$^+$, 8%), 145 (82), 143 (100), 129 (59), 128 (54), 117 (86), 115 (64), 91 (71), 41 (51); HRMS: M$^+$, found 220.1449. $C_{14}H_{20}O_2$ requires 220.1463.

4.4.4. 5,5-Dimethyl-3-phenyl-1,4-hexanediol (11b). Minor isomer:[23] white solid, mp 104–105°C (pentane/dichloromethane); ν (KBr) 3404 (OH), 3085, 3061, 3026 (ArH), 1261 cm^{-1} (C–O); δ_H 0.78 (9H, s, 3CH$_3$), 1.94–2.18 (2H, m, CH$_2$), 2.95 (2H, br s, 2OH), 3.06–3.12 (1H, m, ArCH), 3.36–3.59 (3H, m, C*H*$_2$OH, C*H*OH), 7.19–7.36 (5H, m, ArH); δ_C 26.7 [C(*C*H$_3$)$_3$], 36.0 [*C*(CH$_3$)$_3$], 39.0 (*C*H$_2$CH$_2$OH), 43.7 (ArCH), 60.8 (CH$_2$OH), 82.6 (CHOH), 126.6, 128.3, 129.7, 141.6 (ArC); *m/z* 204 (M$^+$−H$_2$O, 1%), 118 (100), 117 (74), 91 (50); HRMS: M$^+$−H$_2$O, found 204.1519. $C_{14}H_{20}O$ requires 204.1514. Major isomer: colourless liquid; ν (film) 3384 (OH), 3083, 3057, 3027 (ArCH), 1265 cm^{-1} (C–O); δ_H 0.87 (9H, s, 3CH$_3$), 1.83–2.26 (2H, m, C*H*$_2$CH$_2$OH), 2.58 (2H, br s, 2OH), 2.95–3.02 (1H, m, ArCH), 3.36–3.44 (3H, m, C*H*$_2$OH, C*H*OH), 7.16–7.28 (5H, m, ArH); δ_C 26.6 (CH$_3$), 34.2 [*C*(CH$_3$)$_3$], 36.4 (*C*H$_2$CH$_2$OH), 44.6 (ArCH), 61.0 (CH$_2$OH), 82.7 (CHOH), 126.2, 127.1, 128.5, 145.7 (ArC); *m/z* 204 (M$^+$−H$_2$O, 0.5%), 118 (100), 117 (75), 91 (51); HRMS: M$^+$−H$_2$O, found 204.1521. $C_{14}H_{20}O$ requires 204.1514.

4.4.5. 1,2-Diphenyl-1,4-butanediol (11c). Colourless oil; ν (film) 3383 cm^{-1} (OH), 3084, 3061, 3028 (ArH), 1260 cm^{-1} (C–O); δ_H 1.99–2.29 (2H, m, CH$_2$), 2.86 (2H, br s, 2OH), 3.06–3.13 (1H, m, ArCH$_2$), 3.44–3.65 (2H, m, C*H*$_2$OH), 4.82 (1H, d, J=6.7 Hz, C*H*OH), 7.05–7.37 (10H, m, ArH); δ_C 33.8 (*C*H$_2$CH$_2$OH), 50.9 (ArCH), 61.4 (CH$_2$OH), 78.5 (CHOH), 126.4, 126.6, 127.4, 128.0, 128.3, 128.6, 141.6, 142.9 (ArC); *m/z* 242 (M$^+$, 0.5%), 118 (100), 117 (80), 107 (79), 79 (55), 77 (50); HRMS: M$^+$, found 242.1315. $C_{16}H_{18}O_2$ requires 242.1307.

4.4.6. 1-(2-Furyl)-2-phenyl-1,4-butanediol (11d). Major isomer: pale yellow oil; ν (film) 3354 (OH), 3054, 3028 (ArH), 1265 cm^{-1} (C–O); δ_H 1.59 (2H, br s, 2OH), 1.79–1.88 (2H, m, C*H*$_2$CH$_2$OH), 3.26–3.54 (3H, m, C*H*$_2$OH, ArC*H*), 4.84 (1H, d, *J*=8.5 Hz, C*H*OH), 6.24 (1H, d, *J*=3.1 Hz, HC=C*H*O), 6.33 (1H, dd, *J*=3.1, 1.8 Hz, *H*C=CHO), 7.23–7.41 (6H, m, ArH, *H*C=CO); δ_C 34.9 (*C*H$_2$CH$_2$OH), 48.3 (ArCH), 60.8 (CH$_2$OH), 71.8 (CHOH), 107.8, 110.2, 127.3, 128.6, 128.8, 140.4, 142.1, 154.7 (ArC, OC=CHCH=CHO); *m/z* 214 (M$^+$−H$_2$O, 5%), 118 (79), 117 (66), 97 (100); HRMS: M$^+$−H$_2$O, found 214.0988. C$_{14}$H$_{14}$O$_2$ requires 214.0994. Minor isomer: colourless oil; ν (film) 3403 (OH), 3055 (ArH), 1266 cm^{-1} (C–O); δ_H 1.62 (2H, br s, 2OH), 1.99–2.09 (1H, m, C*H*HCH$_2$OH), 2.21–2.32 (1H, m, CH*H*CH$_2$OH) 3.26–3.33 (1H, m, ArCH), 3.48–3.68 (2H, m, C*H*$_2$OH), 4.85 (1H, d, *J*=7.5 Hz, C*H*OH), 6.01 (1H, d, *J*=3.3 Hz, HC=C*H*O), 6.19 (1H, dd, *J*=3.3, 1.8 Hz, *H*C=CHO), 7.12–7.29 (6H, m, ArH, *H*C=CO); δ_C 34.4 (*C*H$_2$CH$_2$OH), 48.4 (ArCH), 61.2 (CH$_2$OH), 72.1 (CHOH), 106.9, 110.0, 126.7, 128.2, 128.4, 141.3, 141.6, 155.1 (ArC, OC=CHCH=CHO), *m/z* 214 (M$^+$−H$_2$O, 4%), 118 (81), 117 (68), 97 (100); HRMS: M$^+$−H$_2$O, found 214.0987. C$_{14}$H$_{14}$O$_2$ requires 214.0994.

4.4.7. 4-Methyl-3-phenyl-1,4-pentanediol (11e). White solid, mp >300°C (pentane/dichloromethane); [Found: C, 74.12; H, 9.25. C$_{12}$H$_{18}$O$_2$ requires C, 74.18; H, 9.34]; ν (KBr) 3384 (OH), 3084, 3054, 3029 (ArH), 1265 cm^{-1} (C–O); δ_H 1.16 (3H, s, CH$_3$), 1.17 (3H, s, CH$_3$), 1.93–2.27 (2H, m, CH$_2$), 2.36 (2H, br s, 2OH), 2.76 (1H, dd, *J*=10.4, 4.0 Hz, ArCH), 3.33–3.58 (2H, m, CH$_2$OH), 7.20–7.32 (4H, m, ArH); δ_C 27.0, 28.7 (CH$_3$), 32.7 (CH$_2$), 53.7 (ArCH), 61.4 (CH$_2$OH), 72.7 (COH), 126.7, 128.2, 129.3, 141.3 (ArC); *m/z* 176 (M$^+$−H$_2$O, 1%), 118 (100), 117 (96), 59 (87), 43 (55).

4.4.8. 4-Pentyl-3-phenyl-1,4-nonanediol (11f). Colourless oil; ν (film) 3403 (OH), 3084, 3058, 3027 (ArH), 1265 cm^{-1} (C–O); δ_H 0.84 (3H, t, *J*=7.2 Hz, CH$_3$), 0.90 (3H, t, *J*=6.8 Hz, CH$_3$), 1.12–1.34 (14H, m, 7CH$_2$), 1.51–1.54 (2H, m, CH$_2$), 1.74 (2H, br s, 2OH), 1.98–2.06 (2H, m, ArCHC*H*$_2$), 2.82 (1H, dd, *J*=9.9, 5.0 Hz, ArCH), 3.29 (1H, td, *J*=10.9, 7.4 Hz, C*H*HOH), 3.46 (1H, td, *J*=10.9, 5.5 Hz, CH*H*OH), 7.19–7.29 (5H, m, ArH); δ_C 14.0, 14.0 (CH$_3$), 22.5, 22.6, 23.0, 23.2, 32.1, 32.3, 32.5, 36.4, 37.3 (CH$_2$), 49.3 (ArCH), 61.3 (CH$_2$OH), 76.0 (COH), 126.5, 128.1, 129.6, 141.0 (ArC); *m/z* 288 (M$^+$−H$_2$O, 0.38%), 171 (99), 118 (74), 55 (70), 43 (100), 41 (62); HRMS: M$^+$−H$_2$O, found 288.2440. C$_{20}$H$_{32}$O requires 288.2453.

4.4.9. 1,1,2,-Triphenyl-1,4-butanediol (11g). White solid, mp 228–230°C (pentane/dichloromethane); [Found: C, 82.57; H, 6.95. C$_{22}$H$_{22}$O$_2$ requires C, 82.98; H, 6.97]; ν (KBr) 3370 (OH), 3085, 3055, 3025 (ArH), 1260 cm^{-1} (C–O); δ_H 2.03–2.07 (2H, m, C*H*$_2$CH$_2$OH), 2.79 (2H, br s, 2OH), 3.34–3.42, 3.51–3.58 (2H, 2m, C*H*$_2$OH), 4.02 (1H, t, *J*=7.3 Hz, ArCH), 6.98–7.15 (7H, m, ArH), 7.22–7.26 (4H, m, ArH), 7.36 (2H, t, *J*=7.6 Hz, ArH), 7.63 (2H, d, *J*=7.3 Hz, ArH); δ_C 33.3 (*C*H$_2$CH$_2$OH), 50.3 (ArCH), 60.9 (CH$_2$OH), 80.7 (COH), 125.7, 126.2, 126.3, 126.6, 126.8, 127.6, 128.0, 128.3, 130.1, 139.5, 145.9, 146.2 (ArC); *m/z* 300 (M$^+$−H$_2$O, 2%), 118 (100), 117 (62).

4.4.10. 1-(3-Hydroxy-1-phenylpropyl)cyclopentanol (11h). White solid, mp 93–94°C (pentane/dichloromethane); [Found: C, 76.25; H, 9.22. C$_{14}$H$_{20}$O$_2$ requires C, 76.31; H, 9.16]; ν (KBr) 3381 (OH), 3084, 3059, 3026 (ArH), 1265 cm^{-1} (C–O); δ_H 1.55–1.80 (8H, m, 4CH$_2$), 2.03–2.18 (2H, m, CH$_2$), 2.79 (1H, dd, *J*=10.1, 4.8 Hz, ArCH), 3.05 (2H, br s, 2OH), 3.33–3.41 (1H, m, C*H*HOH), 3.53 (1H, ddd, *J*=10.7, 6.6, 5.0 Hz, CH*H*OH), 7.20–7.32 (5H, m, ArH); δ_C 23.3, 23.6, 33.4, 38.5, 39.2 (CH$_2$), 51.8 (ArCH), 61.2 (CH$_2$OH), 84.6 (COH), 126.6, 128.2, 129.0, 141.7 (ArC); *m/z* 202 (M$^+$−H$_2$O, 1.8%), 118 (100), 117 (57).

4.4.11. 1-(3-Hydroxy-1-phenylpropyl)cyclohexanol (11i). White solid, mp 119–120°C (pentane/dichloromethane); [Found: C, 76.21; H, 9.46. C$_{15}$H$_{22}$O$_2$ requires C, 76.87; H, 9.47]; ν (KBr) 3333 (OH), 3082, 3060, 3024 (ArH), 1275 cm^{-1} (C–O); δ_H 1.07–1.71 (10H, m, 5CH$_2$), 1.93–2.22 (4H, m, CH$_2$, 2OH), 2.72 (1H, dd, *J*=11.0, 3.7 Hz, ArCH), 3.29–3.37, 3.47–3.54 (2H, 2m, C*H*$_2$OH), 7.22–7.31 (5H, m, ArH); δ_C 21.7, 21.9, 25.6, 31.8, 35.1, 35.8 (CH$_2$), 53.0 (ArCH), 61.4 (CH$_2$OH), 73.0 (COH), 126.5, 128.1, 129.6, 141.1 (ArC); *m/z* 234 (M$^+$, 0.5%), 118 (100), 117 (57), 99 (96), 81 (69).

4.4.12. (1*R*,2*S*,5*R*)-1-(3-Hydroxy-1-phenylpropyl)-2-isopropyl-5-methylcyclohexanol (11j). Major isomer: colourless oil; ν (film) 3394 (OH), 3086, 3053, 3028 (ArH), 1265 cm^{-1} (C–O); δ_H 0.69 (3H, d, *J*=6.8 Hz, CHC*H*$_3$), 0.89 (3H, d, *J*=6.4 Hz, CH$_3$CHC*H*$_3$), 0.92 (3H, d, *J*=6.8 Hz, C*H*$_3$CHCH$_3$), 1.18–1.41 (4H, m, CH$_2$, 2CH), 1.62–1.66 (2H, m, CH$_2$), 1.79–1.96 (2H, m, CH$_2$), 2.24–2.33 (4H, m, CH$_2$, 2OH), 2.44–2.53 (1H, m, CH), 3.35 (1H, dd, *J*=3.9, 3.7 Hz, ArCH), 3.33–3.43 (1H, m, CH*H*OH), 3.56 (1H, ddd, *J*=10.7, 6.3, 4.4 Hz, C*H*HOH), 7.19–7.28 (5H, m, ArH); δ_C 18.4 (CH$_3$), 21.2 (CH$_2$), 22.6, 22.8 (CH$_3$), 25.0, 28.0 (CH), 33.0, 34.4, 41.4 (CH$_2$), 45.8, 49.7 (CH), 61.8 (CH$_2$OH), 78.1 (COH), 126.4, 128.0, 129.6, 141.7 (ArC); *m/z* 290 (M$^+$, 0.5%), 155 (100), 118 (57), 81 (95), 55 (51), 43 (62), 41 (67); HRMS: M$^+$, found 290.2247. C$_{19}$H$_{30}$O$_2$ requires 290.2246. Minor isomer: colourless oil; ν (film) 3404 (OH), 3085, 3054, 3030 (ArH), 1265 cm^{-1} (C–O); δ_H 0.70 (3H, d, *J*=7.0 Hz, C*H*CH$_3$), 0.90 (3H, d, *J*=6.3 Hz, CH$_3$CHC*H*$_3$), 0.93 (3H, d, *J*=6.8 Hz, C*H*$_3$CHCH$_3$), 1.18–1.98 (13H, m, 4CH$_2$, 3CH, 2OH), 2.24–2.35 (1H, m, C*H*HCH$_2$OH, 2.45–2.54 (1H, m, CH*H*CH$_2$OH), 3.33 (1H, dd, *J*=10.1, 4.2 Hz, ArCH), 3.44 (1H, ddd, *J*=10.8, 8.5, 5.5 Hz, CH*H*OH), 3.57 (1H, ddd, *J*=10.8, 6.6, 4.7 Hz, C*H*HOH), 7.21–7.29 (5H, m, ArH); δ_C 18.4 (CH$_3$), 21.2 (CH$_2$), 22.6, 22.8 (CH$_3$), 25.0, 28.1 (CH), 33.2, 34.4, 41.5 (CH$_2$), 45.8, 49.9 (CH), 62.3 (CH$_2$OH), 78.1 (COH), 126.4, 128.1, 129.5, 141.8 (ArC); *m/z* 290 (M$^+$, 0.5%), 155 (87), 118 (57), 81 (100), 43 (56), 41 (64); HRMS: M$^+$, found 290.2250. C$_{19}$H$_{30}$O$_2$ requires 290.2246.

4.5. Reductive opening of 2,3-benzofuran (12)[19]

*Isolation of 2-vinylphenol (**14**).* To a blue suspension of lithium powder (140 mg, 20 mmol) and a catalytic amount of DTBB (50 mg, 0.19 mmol; 5% molar) in THF (4 mL) was added 2,3-benzofuran (**12**, 236 mg, 0.22 mL, 2.0 mmol) at 0°C and the resulting mixture was stirred for 45 min at the same temperature. Then, it was cooled down at −78°C and 0.5 mL of H$_2$O was added and after 15 min it was hydrolysed with 3N hydrochloric acid. The reaction mixture was allowed to reach the ambient temperature and it was extracted with ethyl acetate (3×20 mL), the organic layer dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield 2-vinylphenol (**14**, 93%), which was characterised by comparison of its spectroscopic data with those described in the literature.[19]

4.6. Reductive opening of 4*H*-chromene (15)

*Isolation of 3-phenylpropanal (**18**) and 2-allylphenol (**19**).* To a blue suspension of lithium powder (140 mg, 20 mmol) and a catalytic amount of DTBB (50 mg, 0.19 mmol; 5% molar) in THF (4 mL) was added 4*H*-chromene (**15**, 264 mg, 0.30 mL, 2.0 mmol) at 0°C and the resulting mixture was allowed to reach 20°C. The reaction mixture was stirred for 45 min at the same temperature. Then, it was cooled down at −78°C and 0.5 mL of H_2O was added and after 15 min it was hydrolysed with 3N hydrochloric acid. The reaction mixture was allowed to reach the ambient temperature and it was extracted with ethyl acetate (3×20 mL), the organic layer dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield 3-phenylpropanal (**18**) and 2-allylphenol (**19**) (95%, molar ratio: 2:1, respectively), which were characterised by comparison of their spectroscopic data with those reported in the literature.[21]

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