$ZnBr_2$/CuCN-Promoted, Highly Regioselective S_N2' Reactions of Some Functionalised Organolithium Compounds with Allylic and Propargylic Halides

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Treatment of lithium (2-lithiomethylphenyl)methoxide (**2a**) and lithium 2-(2-lithiomethylphenyl)ethoxide (**2b**) [easily prepared by ring opening of phthalan (**1a**) and isochroman (**1b**), respectively, by the use of lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB)] with zinc bromide and copper cyanide, both in equimolecular amounts, in THF at room temperature, followed by treatment with different allylic chlorides or bromides **3** at –78 or 20 °C, almost exclusively provides (after hydrolysis with water) the corresponding alcohols **4′** resulting from an S_N2' displacement, the process being highly regioselective. The same procedure with intermediates **2a** and **2b** was applied to propargylic chlorides or bromides **5**, exclusively yielding the corresponding allenylic alcohols **6′**, resulting from an S_N2' reaction.

Introduction

From a synthetic point of view, the construction of polyfunctionalised molecules through the creation of carbon-carbon bonds should involve fragments already containing some functionality. In polar reactions this is fairly common, involving electrophilic fragments (bearing positively polarised carbon atoms), but more difficulties are presented in the case of nucleophilic fragments, especially concerning organometallic reagents. Thus, the use of functionalised organometallic compounds[1] presents some problems, because the carbon-metal bond should be compatible with the functionality present in the structure. Two types of this family of intermediates can be found in the literature: (a) systems derived from not too electropositive metals, such as zinc, which are fairly stable and tolerant of different functionalities, but consequently not very reactive and frequently needing to be activated, generally by the use of a transition metal (e.g. nickel or palladium), and (b) intermediates derived from strongly electropositive metals, such as lithium, which are far more reactive than the zinc derivatives, but are less tolerant to functionalities and in many cases have to be generated at low temperatures and used without isolation. Thus, functionalised organolithium compounds[2] are useful reagents for transferring functionality to a wide range of electrophilic reagents to give polyfunctionalised molecules directly. In the last few years, we have been preparing these intermediates by means of an arene-catalysed lithiation[3] under very mild reaction conditions, starting from halogenated[2–4] or non-halogenated[5] materials such as heterocyclic compounds.[6] Recently, we have reported the transformation of the described functionalised organolithium compounds into the corresponding zinc derivatives by treatment with anhydrous zinc bromide, and their reactivity toward α,β-unsaturated carbonyl compounds[7a] and in the Negishi-type coupling reaction.[7b,7c] In this way it is possible to modulate the reactivity of the corresponding functionalised organometallic intermediates, thus making possible reactions such as conjugate addition or cross-coupling, which cannot be performed directly with the original organolithium compounds. In this paper we report the S_N2' reaction of these functionalised organozinc intermediates with different allylic and propargylic halides.

Results and Discussion

Treatment of the organolithium compound **2a** [easily prepared from phthalan by treatment with lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB)][8] with cinnamyl chloride (**3a**) in THF either at −78 °C or at room temperature almost exclusively afforded the corresponding S_N2 product **4a**, the chemical yield being higher at low temperature (Scheme 1 and Table 1, Entries 1 and 2). When one equivalent of anhydrous zinc bromide was added after the formation of the intermediate **2a**, the same procedure, both at low and at room temperature, after final hydrolysis, exclusively gave the "reduced" product (2-methylphenyl)methanol, resulting from metal-hydrogen exchange (Table 1, Entries 3 and 4). We then studied the use of copper cyanide (as the more soluble form CuCN·2LiCl) either in catalytic (Table 1, Entry 5) or stoichiometric amount (Table 1, Entries 6 and 7), working in the last case either at

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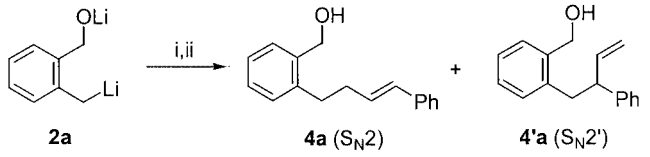
low temperature or at room temperature. Whereas the main product with catalytic (10%) amounts of the copper salt was **4a** (S_N2 reaction product), the major product in the other cases (stoichiometric amount of the copper salt) was **4′a** (S_N2' reaction product). Finally, we considered the possibility of using a combination of both metallic salts, so zinc bromide was used in equimolar amount and copper(I) cyanide either in catalytic (10%) or in equimolar amounts in the reaction shown in Scheme 1, both at −78 °C and at room temperature (Table 1, Entries 8−11). In all cases the corresponding product **4′a**, resulting from a S_N2' reaction, was obtained almost exclusively.[9] Although no important differences were found, the best conditions are shown in Table 1, Entry 11: one equivalent of each metallic salt and −78 °C.



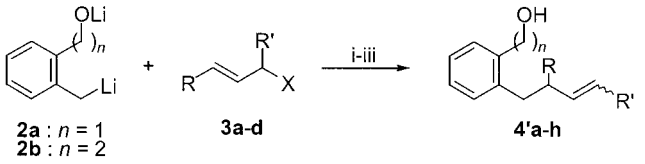
Scheme 1. Reagents: (i) (*E*)-PhCH=CHCH$_2$Cl, with or without $ZnBr_2$, and CuCN·2LiCl (conditions given in Table 1), THF, 1 h; (ii) H_2O, then 3 M HCl

Table 1. S_N2 versus S_N2' allylation of organolithium compound **2a** with cinnamyl chloride

Entry	Additive		Temperature (°C)	Products **4a**/**4′a**	
	$ZnBr_2$ (equiv.)	CuCN·2LiCl (equiv.)		S_N2:S_N2'[a]	Yield (%)[b]
1	−	−	20	95:5	52
2	−	−	−78	97:3	81
3	1	−	20	−[c]	<1
4	1	−	−78	−[c]	<1
5	−	0.1	20	92:8	58
6	−	1	20	38:62	62
7	−	1	−78	29:71	43
8	1	0.1	20	5:95	31
9	1	0.1	−78	5:95	49
10	1	1	20	5:95	50
11	1	1	−78	4:96	57

[a] Determined by 300 MHz ^{1}H NMR from the reaction crude. [b] Isolated yield of **4a** + **4′a** after column chromatography (silica gel, hexane/ethyl acetate). [c] Only (2-methylphenyl)methanol (> 90%) was obtained.

With the results described above in hand, we studied the reactions of functionalised organolithium compounds **2a** and **2b** (the latter being easily prepared by reductive ring-opening of isochroman under the same reaction conditions as used for **2a**)[10] under the best conditions indicated previously. Thus, with different allylic halides **3a**−**d**, both starting materials gave the expected S_N2' products **4′a**−**h** either exclusively or as very major products (Scheme 2 and Table 2). In general, regioselectivities and yields are fairly similar at low temperature and at room temperature, being slightly higher at −78 °C (compare Entries 1 and 2, 3 and 4, 7 and 8, and 10 and 11 in Table 2).

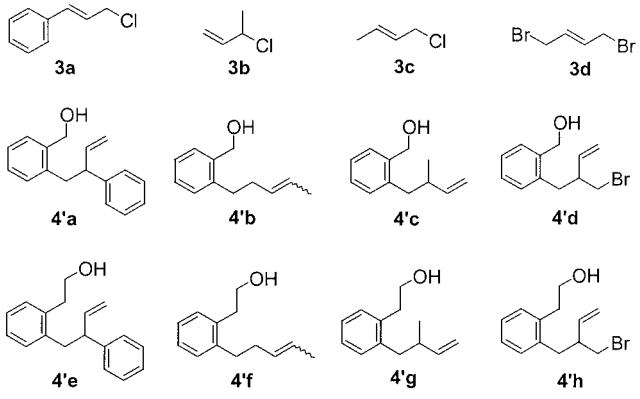


Scheme 2. Reagents: (i) $ZnBr_2$, CuCN·2LiCl, THF, 0 or 20 °C, 10 min; (ii) **3**, −78 or 20 °C, 1 h; (iii) H_2O, then 3 M HCl

Table 2. Reactions between compounds **2** and allylic halides **3** in the presence of $ZnBr_2$/CuCN·2LiCl

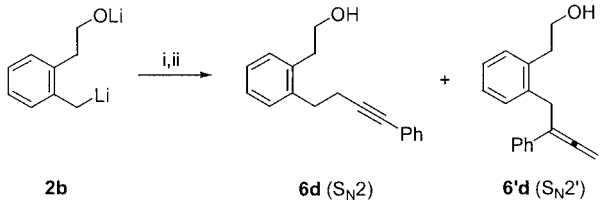
Entry	Starting material	Allylic halide	Temperature (°C)	Product[a]		
				No.	S_N2':S_N2 [b]	Yield (%)[c]
1	**2a**	**3a**	−78	**4′a**	96:4	57
2			20		95:5	51
3	**2a**	**3b**	−78	**4′b**	100:0[d]	61
4			20		100:0[e]	42
5	**2a**	**3c**	−78	**4′c**	92:8	71
6	**2a**	**3d**	−78	**4′d**	100:0	62
7	**2b**	**3a**	−78	**4′e**	96:4	50
8			20		90:10	63
9	**2b**	**3b**	−78	**4′f**	100:0 [e]	55
10	**2b**	**3c**	−78	**4′g**	92:8	53
11			20		90:10	60
12	**2b**	**3d**	−78	**4′h**	100:0	49

[a] All products **4′** were > 90% pure (GLC and 300 MHz ^{1}H NMR). [b] Determined by 300 MHz ^{1}H NMR from the crude reaction mixture. [c] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the heterocyclic starting material (phthalan for **2a** and isochroman for **2b**). [d] 1:3 *Z*/*E* diastereomeric mixture (300 MHz ^{1}H NMR). [e] 1:2.4 *Z*/*E* diastereomeric mixture (300 MHz ^{1}H NMR).



The functionalised organolithium compound **2b** was chosen in order to study the best reaction conditions in its reaction with 3-phenylpropargyl chloride (**5a**) (Scheme 3). In the absence of any additive, only S_N2 product **6d** was obtained after 1 h reaction time at −78 °C and subsequent hydrolysis (Table 3, Entry 1). With one equivalent of zinc bromide the only reaction product was the corresponding "reduced" compound [2-(2-methylphenyl)ethanol], re-

sulting from a metal-hydrogen exchange (Table 3, Entry 2). When one equivalent of copper cyanide was used as the additive, only S_N2' product (**6′d**) was isolated but the yield was moderate (Table 3, Entry 3). Finally, the combined use of both metallic salts gave the best result (Table 3, Entry 4).[11] In all cases the rest of the starting material was converted into the described "reduced" product, which could easily be separated from the desired product **6′d**.



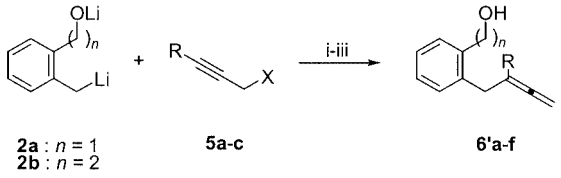
Scheme 3. Reagents: (i) $PhC{\equiv}CCH_2Cl$, with or without $ZnBr_2$, and CuCN·2LiCl (conditions given in Table 3), THF, −78 °C, 1 h; (ii) H_2O, −78 to 20 °C, then 3 M HCl

Table 3. S_N2 versus S_N2' propargylation of organolithium compound **2b** with 3-phenylpropargyl chloride

Entry	Additive		Products **6d/6′d**	
	$ZnBr_2$ (equiv.)	CuCN·2LiCl (equiv.)	$S_N2:S_N2'$ [a]	Yield (%)[b]
1	–	–	100:0	51
2	1	–	–	<1[c]
3	–	1	0:100	39
4	1	–	0:100	57

[a] Determined by 300 MHz ^{1}H NMR from the reaction crude. [b] Isolated yield of **6d** or **6′d** after column chromatography (silica gel, hexane/ethyl acetate). [c] Only 2-(2-methylphenyl)ethanol (> 90%) was obtained.

Once the best reaction conditions were known, the reaction was carried out with the two functionalised organolithium compounds **2a** and **2b** and with different propargylic halides **5**, so the corresponding functionalised allenes **6′a−f**, together with variable amounts of the "reduced" alcohols (resulting from a metal-hydrogen exchange), were the only reaction products isolated (Scheme 4 and Table 4).

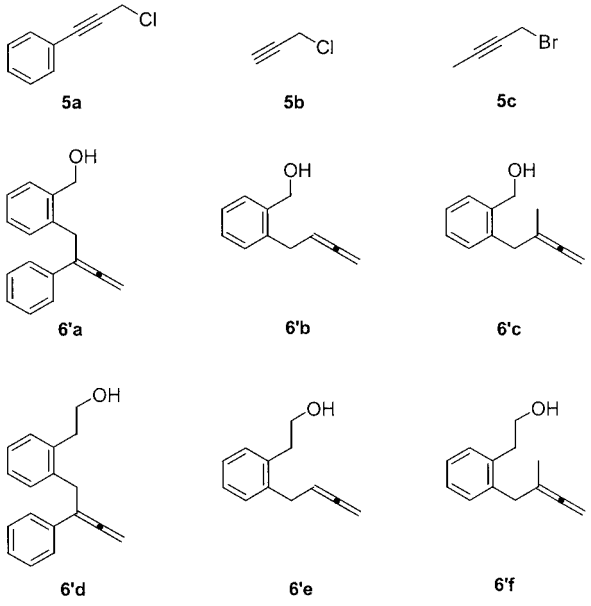


Scheme 4. Reagents: (i) $ZnBr_2$, CuCN·2LiCl, THF, 0 or 20 °C, 10 min; (ii) **5**, −78 °C, 1 h; (iii) H_2O, then 3 M HCl

Table 4. Reactions between compounds **2** and propargylic halides **5** in the presence of $ZnBr_2$/CuCN·2LiCl

Entry	Starting material	Propargylic halide	Product[a]	Yield (%)[b]
1	**2a**	**5a**	**6′a**	45
2	**2a**	**5b**	**6′b**	51
3	**2a**	**5c**	**6′c**	59
4	**2b**	**5a**	**6′d**	57
5	**2b**	**5b**	**6′e**	49
6	**2b**	**5c**	**6′f**	60

[a] All products **6′** were > 95% pure (GLC and 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the heterocyclic starting material (phthalan for **2a** and isochroman for **2b**).



Conclusions

In conclusion, the combined use of zinc bromide and copper(I) cyanide, both in stoichiometric amounts, allows allylic and propargylic substitution with different allylic and propargylic chlorides and bromides to be directed toward the S_N2' process in a very efficient and regioselective manner. In the absence of both metallic salts the process either proceeds by an S_N2 pathway or it does not work.

Experimental Section

General: All reactions were carried out under argon. FT-IR spectra were obtained with a Nicolet Impact 400D spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, with a Bruker AC 300 with $CDCl_3$ as solvent and TMS as internal standard; chemical shifts (δ) are given in ppm and coupling constants (*J*) are given in Hz. Low-resolution mass spectra (EI) were obtained at 70 eV with an Agilent 5973 Network spectrometer, fragment ions in *m*/*z* with relative intensities (%) in par-

entheses. High-resolution mass spectra were obtained by the corresponding service at the University of Alicante on a Finnigan MAT 95 S apparatus. The purities of volatile products and chromatographic analyses (GLC) were determined with a Hewlett−Packard HP−4890 instrument equipped with a flame ionisation detector and a 30 m capillary column (0.25 mm diam., 0.25 μm film thickness), with nitrogen (2 mL/min) as carrier gas, $T_{injector}$ = 275 °C, T_{column} = 80 °C (3 min) and 80−270 °C (15 °C/min). Thin layer chromatography (TLC) was carried out on Merck plastic sheets coated with 60 F_{254} silica gel. Column chromatography was carried out over Merck 63−200 μm silica gel. All starting materials and solvents were commercially available (Acros, Aldrich, Fluka) and were used as the best grade without further purification. Lithium powder was prepared from commercially available lithium granules (99%, high sodium content, Aldrich) as already reported by us.[12] Zinc bromide was dried by heating at 130 °C under reduced pressure (0.1 Torr) for 2 h before use. 3-Phenylpropargyl chloride was prepared by the reported procedure.[13]

DTBB-Catalysed Lithiation of Isochroman (1a) and Phthalan (1b), and Copper-Mediated S_N2' Reaction with Allylic and Propargylic Chlorides and Bromides. Isolation of Compounds 4, 4′ and 6, 6′. General Procedure: Phthalan (**1a**) or isochroman (**1b**) (2 mmol) was added dropwise, either at 0 °C (for **1a**) or at room temperature (for **1b**), under argon, to a stirred green suspension of lithium powder (70 mg, 10 mmol) and DTBB (53 mg, 0.2 mmol) in THF (10 mL). The colour disappeared after the addition, and reappeared after 45 min stirring. The excess of lithium was then filtered off using inert conditions and the resulting solution was added to a solution of zinc bromide (450 mg, 2 mmol) in THF (5 mL). A solution of CuCN·2LiCl [prepared by dissolving copper(I) cyanide (180 mg, 2 mmol) and lithium chloride (85 mg, 4 mmol) in THF (10 mL)] was added to the resulting mixture, which was then cooled to −78 °C. After 10 min stirring, the corresponding allylic or propargylic halide (2.2 mmol) was added. After 1 h stirring at the same temperature the mixture was hydrolysed with water (30 mL), acidified with 3 M HCl (6 mL) and extracted with ether (3 × 10 mL). The organic layer was washed with brine (2 × 10 mL) and dried over $MgSO_4$, and the solvents were evaporated (15 Torr) to yield a residue, which was analysed by GLC and purified by column chromatography (silica gel, hexane/ethyl acetate) to give compounds **4**, **4′** and **6**, **6′**.

2-[(*E*)-4-Phenyl-3-butenyl]phenylmethanol (4a): R_f = 0.31 (hexane/ethyl acetate, 3:1). t_R = 14.88 min. IR (film): $\tilde{\nu}$ = 3670−3125 (OH), 3060, 3025, 1490, 1450 (C=CH), 1005 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.50 (m, 2 H, CH_2CH=CH), 2.82 (t, *J* = 7.9 Hz, 3 H, ArCH_2CH_2C and OH), 4.64 (s, 2 H, CH_2OH), 6.27 (dt, *J* = 15.9, 6.7 Hz, 1 H, CH_2C*H*=CH), 6.43 (d, *J* = 15.9 Hz, 1 H, CH_2CH=C*H*), 7.16−7.38 (m, 9 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.8, 34.2 (2 × CH_2), 62.4 (CH_2OH), 125.7, 126.0, 126.8, 127.6, 127.9, 128.3, 129.1, 129.6, 130.2, 137.4, 138.2, 139.4 (14 C, C=C and ArC) ppm. GC-LRMS: *m*/*z* (%) = 238 (2.0) [M^+], 129 (17), 118 (10), 117 (100), 116 (81), 115 (43), 93 (10), 91 (41), 77 (17). HRMS for $C_{17}H_{18}O$: calcd. 238.1358; found 238.1372 [M^+].

2-(2-Phenyl-3-butenyl)phenylmethanol (4′a): R_f = 0.25 (hexane/ethyl acetate, 3:1). t_R = 13.39 min. IR (film): $\tilde{\nu}$ = 3683−3131 (OH), 3065, 3026, 1490, 1451 (C=CH), 1004 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 (br. s, 1 H, OH), 3.01−3.15 (m, 2 H, ArCH_2CH), 3.58 (q, *J* = 7.3 Hz, 1 H, CH), 4.53 (s, 2 H, CH_2OH), 4.98 (d, *J* = 17.1 Hz, 1 H, CH=C*H*H), 5.04 (d, *J* = 10.4 Hz, 1 H, CH=CH*H*), 6.08 (ddd, *J* = 17.1, 10.4, 7.3 Hz, 1 H, C*H*=CH_2), 7.05−7.37 (m, 9 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.4 (Ar*C*H_2CH), 51.3 (CH), 63.0 (CH_2OH), 114.9, 141.0 (C=C), 126.4, 127.6, 127.8, 128.4, 130.4, 138.1, 138.7, 143.5 (12 C, ArC) ppm. GC-LRMS: *m*/*z* (%) = 238 (0.1) [M^+], 118 (10), 117 (100), 116 (47), 115 (35), 91 (28), 77 (12). HRMS for $C_{17}H_{18}O$: calcd. 238.1358; found 238.1374 [M^+].

2-(3-Pentenyl)phenylmethanol (4′b): R_f = 0.44 (hexane/ethyl acetate, 3:1). t_R = 9.67 min. IR (film): $\tilde{\nu}$ = 3670−3112 (OH), 3065, 3020, 1450 (C=CH), 1008 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.47 and 1.56 (2d, *J* = 4.3 Hz, 3 H, CH_3), 1.89 (br. s, 1 H, OH), 2.19−2.30 (m, 2 H, CH_2CH=CH), 2.63 (t, *J* = 7.6 Hz, 2 H, ArCH_2CH_2), 4.59 (s, 2 H, CH_2OH), 5.39 (m, 2 H, CH=CH), 7.09−7.16 (m, 3 H, ArH), 7.27 (d, *J* = 6.7 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8 (CH_3), 32.3, 34.1 (CH_2CH_2), 62.9 (CH_2OH), 125.6, 126.1, 127.8, 128.1, 129.3, 130.4, 138.2, 140.1 (C=C and ArC) ppm. GC-LRMS: *m*/*z* (%) = 176 (3.1) [M^+], 158 (20), 143 (39), 130 (26), 129 (66), 128 (22), 121 (24), 120 (16), 119 (17), 117 (14), 116 (85), 115 (20), 104 (23), 103 (15), 93 (99), 92 (11), 91 (100), 78 (1), 77 (68), 65 (16), 55 (19), 51 (11). HRMS for $C_{12}H_{16}O$: calcd. 176.1201; found 176.1172 [M^+].

2-(2-Methyl-3-butenyl)phenylmethanol (4′c): R_f = 0.37 (hexane/ethyl acetate, 3:1). t_R = 9.03 min. IR (film): $\tilde{\nu}$ = 3689−3125 (OH), 3071, 3022, 1486, 1454 (C=CH), 1004 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.01 (d, *J* = 6.7 Hz, 3 H, CH_3), 2.16 (br. s, 1 H, OH), 2.37−2.74 (m, 3 H, ArCH_2CH), 4.63 (s, 2 H, CH_2OH), 4.88−4.93 (m, 2 H, CH=CH_2), 5.77 (ddd, *J* = 17.7, 10.4, 7.1 Hz, 1 H, C*H*=CH_2), 7.12−7.35 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5 (CH_3), 39.0 (CH), 39.2 (Ar*C*H_2CH), 62.8 (CH_2OH), 112.9, 143.6 (C=C), 126.1, 127.4, 128.1, 130.3, 138.5, 138.6 (ArC) ppm. GC-LRMS: *m*/*z* (%) = 176 (4.2) [M^+], 158 (20), 143 (35), 130 (15), 129 (36), 128 (18), 121 (43), 120 (22), 119 (12), 116 (23), 115 (16), 104 (24), 103 (13), 93 (100), 92 (10), 91 (90), 78 (13), 77 (60), 65 (15), 55 (14), 51 (11). HRMS for $C_{12}H_{16}O$: calcd. 176.1201; found 176.1207 [M^+].

2-(2-Bromomethyl-3-butenyl)phenylmethanol (4′d): R_f = 0.26 (hexane/ethyl acetate, 3:1). t_R = 12.03 min. IR (film): $\tilde{\nu}$ = 3676−3135 (OH), 3072, 3022, 1486, 1450 (C=CH), 1018 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.75 (br. s, 1 H, OH), 2.69−3.04 (m, 3 H, ArCH_2CH), 3.36−3.47 (m, 2 H, CH_2Br), 4.71 (s, 2 H, CH_2OH), 5.03 (d, *J* = 17.3 Hz, 1 H, CH=C*H*H), 5.09 (d, *J* = 10.6 Hz, 1 H, CH=CH*H*), 5.75 (ddd, *J* = 17.3, 10.6, 7.4 Hz, 1 H, C*H*=CH_2), 7.19−7.39 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.4, 37.7 (CH_2Ar and CH_2Br), 46.4 (CH), 63.1 (CH_2OH), 117.0, 138.8 (C=C), 126.7, 127.9, 128.7, 130.4, 137.3, 138.7 (ArC) ppm. GC-LRMS: *m*/*z* (%) = 254 (1.7) [M^+], 157 (43), 129 (23), 128 (18), 121 (100), 120 (18), 119 (15), 115 (19), 103 (13), 93 (88), 91 (82), 78 (11), 77 (51), 65 (13), 53 (14), 51 (10). HRMS for $C_{12}H_{15}BrO$: calcd. 254.0306; found 254.0289 [M^+].

2-[2-(2-Phenyl-3-butenyl)phenyl]ethanol (4′e): R_f = 0.34 (hexane/ethyl acetate, 3:1). t_R = 14.01 min. IR (film): $\tilde{\nu}$ = 3664−3125 (OH), 3063, 3024, 1490, 1451 (C=CH), 1043 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.56 (br. s, 1 H, OH), 2.90 (t, *J* = 6.8 Hz, 2 H, ArCH_2CH_2), 2.97−3.13 (m, 2 H, ArCH_2CH), 3.55 (q, *J* = 7.3 1 H, CH), 3.84 (t, *J* = 6.9 Hz, 2 H, CH_2OH), 4.95 (d, *J* = 17.1 Hz, 1 H, CH=C*H*H), 5.03 (d, *J* = 10.3 Hz, 1 H, CH=CH*H*), 6.08 (ddd, *J* = 17.1, 10.3, 7.3 Hz, 1 H, C*H*=CH_2), 7.02−7.29 (m, 9 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.6, 38.7 (2 × CH_2Ar), 51.1 (CH), 63.3 (CH_2OH), 114.8, 141.0 (C=C), 126.2, 126.4, 127.8, 128.4, 129.6, 130.6, 136.3, 138.4, 143.6 (12 C, ArC) ppm. GC-LRMS: *m*/*z* (%) = 252 (1.2) [M^+], 135 (19), 130 (10), 118 (27), 117 (100), 115 (34), 91 (24). HRMS for $C_{18}H_{20}O$: calcd. 252.1514; found 252.1501 [M^+].

2-[2-(3-Pentenyl)phenyl]ethanol (4′f): R_f = 0.41 (hexane/ethyl acetate, 3:1). t_R = 10.50 min. IR (film): $\tilde{\nu}$ = 3645−3112 (OH), 3062, 3018, 1488, 1448 (C=C), 1045 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.56 and 1.64 (2d, J = 4.2 Hz, 3 H, CH_3), 2.01 (br. s, 1 H, OH), 2.23−2.34 (m, 2 H, CH_2CH=CH), 2.68 (m, 2 H, ArCH_2CH$_2$), 2.89 (t, J = 7.0 Hz, 2 H, ArCH_2CH$_2$OH), 3.80 (t, J = 7.0 Hz, 2 H, CH_2OH), 5.46−5.50 (m, 2 H, CH=CH), 7.15−7.18 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8 (CH_3), 32.7, 34.1 (CH_2CH_2), 63.2 (CH_2OH), 125.4, 125.9, 126.5, 129.3, 129.7, 130.4, 135.9, 140.5 (C=C and ArC) ppm. GC-LRMS: m/z (%) = 190 (14) [M^+], 161 (13), 143 (18), 135 (85), 129 (11), 128 (11), 118 (12), 117 (100), 116 (11), 115 (44), 107 (10), 105 (26), 104 (21), 103 (15), 93 (27), 91 (38), 79 (12), 78 (11), 77 (16). HRMS for $C_{13}H_{18}O$: calcd. 190.1358; found 190.1357 [M^+].

2-[2-(2-Methyl-3-butenyl)phenyl]ethanol (4′g): R_f = 0.42 (hexane/ethyl acetate, 3:1). t_R = 9.87 min. IR (film): $\tilde{\nu}$ = 3651−3112 (OH), 3069, 3018, 1487, 1452 (C=CH), 1045 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, J = 6.7 Hz, 3 H, CH_3), 1.66 (br. s, 1 H, OH), 2.38−2.74 (m, 3 H, ArCH_2CHCH$_3$), 2.90 (t, J = 7.0 Hz, 2 H, ArCH_2CH$_2$), 3.81 (t, J = 7.0 Hz, 2 H, CH_2OH), 4.90−4.96 (m, 2 H, CH=CH_2), 5.80 (ddd, J = 17.1, 10.4, 7.3 Hz, 1 H, CH=CH$_2$), 7.13−7.24 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4 (CH_3), 35.7, 39.3 (2 × CH_2Ar), 38.9 (CH), 63.3 (CH_2OH), 112.8, 143.7 (C=C), 126.1, 126.2, 129.7, 130.5, 136.2, 139.1 (ArC) ppm. GC-LRMS: m/z (%) = 190 (9.3) [M^+], 143 (13), 136 (10), 135 (100), 129 (11), 128 (12), 118 (11), 117 (96), 116 (12), 115 (44), 105 (26), 104 (16), 103 (14), 93 (28), 91 (38), 79 (12), 78 (10), 77 (16). HRMS for $C_{13}H_{18}O$: calcd. 190.1358; found 190.1363 [M^+].

2-[2-(2-Bromomethyl-3-butenyl)phenyl]ethanol (4′h): R_f = 0.30 (hexane/ethyl acetate, 3:1). t_R = 12.68 min. IR (film): $\tilde{\nu}$ = 3626−3125 (OH), 3068, 3018, 1489, 1448 (C=CH), 1045 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.72 (br. s, 1 H, OH), 2.64−2.99 (m, 5 H, 2 × CH_2Ar and CH), 3.41 (t, J = 4.6 Hz, 2 H, CH_2Br), 3.83 (t, J = 6.7 Hz, 2 H, CH_2OH), 5.03 (d, J = 17.7 Hz, 1 H, CH=CHH), 5.10 (d, J = 10.4 Hz, 1 H, CH=CHH), 5.74 (ddd, J = 17.7, 10.4, 7.3 Hz, 1 H, CH=CH$_2$), 7.15−7.19 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.7, 35.8, 37.7 (2 × CH_2Ar and CH_2Br), 46.2 (CH), 63.3 (CH_2OH), 116.9, 138.8 (C=C), 126.4, 126.6, 129.9, 130.5, 136.5, 137.5 (ArC) ppm. GC-LRMS: m/z (%) = 268 (0.1) [M^+], 136 (10), 135 (100), 117 (49), 115 (24), 105 (14), 104 (20), 103 (10), 93 (14), 91 (19). HRMS for $C_{13}H_{17}BrO$: calcd. 268.0463; found 268.0486 [M^+].

2-[2-(4-Phenyl-3-butynyl)]ethanol (6a): R_f = 0.28 (hexane/ethyl acetate, 3:1). t_R = 15.59 min. IR (film): $\tilde{\nu}$ = 3696−3125 (OH), 3060, 3022, 1489, 1443 (C=C), 2230 (C≡C), 1045 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.79 (br. s, 1 H, OH), 2.67 (t, J = 7.5 Hz, 2 H, CH_2C≡C), 2.91−2.99 (m, 4 H, 2 × CH_2Ar), 3.82 (t, J = 6.9 Hz, 2 H, CH_2OH), 7.14−7.38 (m, 9 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CH_2C≡C), 31.7, 35.6 (2 × CH_2Ar), 63.3 (CH_2OH), 81.3, 89.3 (C≡C), 123.6, 126.6, 126.7, 128.1, 129.5, 129.8, 131.4, 136.1, 139.0 (12 C, ArC) ppm. GC-LRMS: m/z (%) = 250 (10) [M^+], 232 (38), 231 (11), 217 (39), 205 (15), 204 (14), 203 (23), 202 (15), 135 (40), 128 (18), 118 (12), 117 (100), 116 (30), 115 (98), 105 (30), 104 (23), 103 (20), 93 (24), 91 (66), 89 (15), 78 (14), 77 (20), 65 (13), 63 (10). HRMS for $C_{18}H_{18}O$: calcd. 250.1358; found 250.1342 [M^+].

2-[2-(2-Phenyl-2,3-butadienyl)phenyl]ethanol (6′a): R_f = 0.29 (hexane/ethyl acetate, 3:1). t_R = 14.76 min. IR (film): $\tilde{\nu}$ = 3683−3125 (OH), 3059, 3025, 1491, 1451 (C=CH), 1940 (C=C=C), 1043 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.65 (br. s, 1 H, OH), 2.92 (t, J = 6.9 Hz, 2 H, ArCH_2CH$_2$OH), 3.80 (t, J = 2.9 Hz, 2 H, ArCH_2C=C), 3.84 (t, J = 6.9 Hz, 2 H, CH_2OH), 4.90 (m, 2 H, =CH$_2$), 7.15−7.23 (m, 5 H, ArH), 7.29−7.34 (m, 2 H, ArH), 7.42−7.44 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.7, 35.9 (2 × CH_2Ar), 63.0 (CH_2OH), 78.7 (=CH_2), 104.7 (C=C=CH_2), 126.0, 126.5, 126.6, 126.8, 128.4, 129.7, 130.2, 136.0, 136.6, 137.5 (12 C, ArC), 209.3 (=C=) ppm. GC-LRMS: m/z (%) = 250 (5.2) [M^+], 233 (17), 232 (89), 231 (23), 219 (12), 218 (21), 217 (99), 216 (21), 215 (32), 208 (38), 204 (41), 203 (58), 202 (54), 191 (13), 190 (10), 189 (14), 178 (16), 165 (11), 140 (19), 129 (16), 128 (25), 127 (12), 117 (64), 116 (22), 115 (100), 105 (31), 104 (17), 103 (29), 102 (12), 101 (11), 93 (11), 91 (89), 89 (21), 79 (15), 78 (18), 77 (33), 65 (18), 63, (14), 51 (15). HRMS for $C_{18}H_{18}O$: calcd. 250.1358; found 250.1399 [M^+].

2-[2-(2,3-Butadienyl)phenyl]ethanol (6′b): R_f = 0.34 (hexane/ethyl acetate, 3:1). t_R = 9.98 min. IR (film): $\tilde{\nu}$ = 3676−3106 (OH), 3063, 3019, 1488, 1449 (C=CH), 1954 (C=C=C), 1044 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.83 (br. s, 1 H, OH), 2.87 (t, J = 6.9 Hz, 2 H, ArCH_2CH$_2$OH), 3.36−3.40 (m, 2 H, ArCH_2CH), 3.80 (t, J = 6.9 Hz, 2 H, CH_2OH), 4.65−4.69 (m, 2 H, =CH$_2$), 5.20−5.29 (m, 1 H, CH=C), 7.11−7.23 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.2, 35.8 (2 × CH_2Ar), 63.1 (CH_2OH), 75.3 (=CH_2), 89.5 (CH=), 126.0, 126.7, 129.5, 129.9, 136.3, 138.5 (ArC), 208.7 (=C=) ppm. GC-LRMS: m/z (%) = 174 (0.1) [M^+], 156 (27), 155 (17), 143 (12), 142 (16), 141 (100), 129 (37), 128 (78), 127 (17), 117 (30), 116 (10), 115 (52), 105 (12), 104 (17), 103 (11), 91 (26), 77 (15). HRMS for $C_{12}H_{14}O$: calcd. 174.1045; found 174.1058 [M^+].

2-[2-(2-Methyl-2,3-butadienyl)phenyl]ethanol (6′c): R_f = 0.34 (hexane/ethyl acetate, 3:1). t_R = 10.24 min. IR (film): $\tilde{\nu}$ = 3664−3106 (OH), 3062, 3019, 1487, 1447 (C=CH), 1960 (C=C=C), 1044 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.66 (t, J = 3.0 Hz, 3 H, CH_3), 1.96 (br. s, 1 H, OH), 2.90 (t, J = 7.0 Hz, 2 H, ArCH_2CH$_2$OH), 3.32 (t, J = 2.9 Hz, 2 H, ArCH_2C(CH_3)], 3.80 (t, J = 7.0 Hz, 2 H, CH_2OH), 4.51−4.53 (m, 2 H, =CH$_2$), 7.16 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.2 (CH_3), 35.7, 37.7 (2 × CH_2Ar), 63.1 (CH_2OH), 74.1 (=CH_2), 97.9 (C=C=CH_2), 126.3, 126.5, 129.8, 130.3, 136.8, 137.6 (ArC), 206.8 (=C=) ppm. GC-LRMS: m/z (%) = 188 (0.4) [M^+], 170 (37), 157 (12), 156 (14), 155 (100), 154 (10), 153 (12), 143 (17), 142 (28), 141 (36), 129 (27), 128 (38), 127 (10), 117 (27), 115 (46), 105 (12), 103 (12), 91 (26), 77 (15). HRMS for $C_{13}H_{16}O$: calcd. 188.1201; found 188.1165 [M^+].

2-(2-Phenyl-2,3-butadienyl)phenylmethanol (6′d): R_f = 0.34 (hexane/ethyl acetate, 3:1). t_R = 14.29 min. IR (film): $\tilde{\nu}$ = 3638−3125 (OH), 3060, 3030, 1491, 1450 (C=CH), 1940 (C=C=C), 1009 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.80 (br. s, 1 H, OH), 3.84 (m, 2 H, ArCH_2C=C), 4.71 (s, 2 H, CH_2OH), 4.90 (m, 2 H, =CH_2), 7.17−7.22 (m, 5 H, ArH), 7.26−7.33 (m, 2 H, ArH), 7.37−7.44 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.2 (ArCH_2C), 63.2 (CH_2OH), 78.6 (=CH_2), 104.5 (C=C=CH_2), 126.0, 126.7, 126.8, 127.8, 128.0, 128.4, 130.0, 135.8, 137.0, 138.8 (12 C, ArC), 209.2 (=C=) ppm. GC-LRMS: m/z (%) = 236 (3.1) [M^+], 218 (13), 217 (17), 215 (12), 206 (17), 205 (41), 204 (19), 203 (27), 202 (33), 193 (12), 191 (12), 190 (10), 178 (14), 145 (17), 144 (20), 128 (15), 127 (11), 117 (27), 116 (17), 115 (48), 105 (10), 103 (14), 93 (11), 91 (100), 89 (15), 77 (37), 65 (12), 63 (10), 51 (12). HRMS for $C_{17}H_{16}O$: calcd. 236.1201; found 236.1200 [M^+].

2-(2,3-Butadienyl)phenylmethanol (6′e): R_f = 0.41 (hexane/ethyl acetate, 3:1). t_R = 9.18 min. IR (film): $\tilde{\nu}$ = 3613−3106 (OH), 3065, 3025, 1449 (C=CH), 1954 (C=C=C), 1011 cm^{-1} (C−O). ^1H NMR

(300 MHz, $CDCl_3$): δ = 1.74 (br. s, 1 H, OH), 3.40−3.45 (m, 2 H, ArCH_2CH), 4.67−4.71 (m, 2 H, =CH_2), 4.72 (s, 2 H, CH_2OH), 5.23−5.32 (m, 1 H, CH=C), 7.17−7.29 (m, 3 H, ArH), 7.33−7.40 (m, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.9 (Ar*C*H_2C), 63.1 (CH_2OH), 75.4 (=CH_2), 89.6 (CH=), 126.7, 128.0, 128.2, 129.6, 138.1, 138.6 (ArC), 208.7 (=C=) ppm. GC-LRMS: *m*/*z* (%) = 160 (1.4) [M^+], 145 (33), 142 (47), 141 (100), 131 (10), 130 (31), 129 (45), 128 (40), 127 (20), 117 (20), 116 (63), 115 (54), 93 (12), 91 (56), 78 (10), 77 (44), 65 (14), 63 (12), 51 (18). HRMS for $C_{11}H_{12}O$: calcd. 160.0888; found 160.0877 [M^+].

2-(2-Methyl-2,3-butadienyl)phenylmethanol (6′f): R_f = 0.41 (hexane/ethyl acetate, 3:1). t_R = 9.42 min. IR (film): ṽ = 3645−3112 (OH), 3064, 3025, 1447 (C=CH), 1960 (C=C=C), 1008 cm^{-1} (C−O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.67 (t, *J* = 3.0 Hz, 3 H, CH_3), 1.84 (br. s, 1 H, OH), 3.36 (t, *J* = 2.9 Hz, 2 H, ArCH_2C(CH_3)], 4.52−4.56 (m, 2 H, =CH_2), 7.16−7.25 (m, 3 H, ArH), 7.37−7.40 (m, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3 (CH_3), 37.4 (Ar*C*H_2C), 63.0 (CH_2OH), 74.3 (=CH_2), 98.1 (*C*=C=CH_2), 126.8, 127.6, 128.2, 130.3, 137.0, 139.1 (ArC), 206.6 (=C=) ppm. GC-LRMS: *m*/*z* (%) = 174 (0.6) [M^+], 160 (10), 159 (88), 156 (16), 155 (20), 145 (16), 144 (35), 143 (37), 142 (19), 141 (97), 131 (42), 130 (22), 129 (88), 128 (100), 127 (26), 119 (12), 117 (12), 116 (24), 115 (56), 103 (14), 93 (24), 91 (83), 89 (12), 78 (15), 77 (63), 65 (22), 63 (14), 51 (22). HRMS for $C_{12}H_{14}O$: calcd. 174.1045; found 174.1031 [M^+].

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