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1,2-Di(lithiomethyl)benzene from Phthalan: Sequential Introduction of Two Different Electrophiles†

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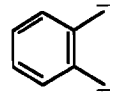
Abstract: The reaction of phthalan (**1**) with an excess of lithium powder and a catalytic amount of DTBB (2.5 mol %) in THF at 20°C followed by treatment with electrophiles (D_2O, CO_2 and carbonyl compounds) at -78°C leads, after hydrolysis, to the corresponding functionalised benzylic alcohols **3a-g**. When the lithiation reaction is continued, after the reaction with the first electrophile, and a second electrophile (H_2O, D_2O and carbonyl compounds) is added, the corresponding disubstituted compounds **6a-q** are prepared. Diols **3c-g** and **6h,i,l,n** and hydroxyacids **6a,c,f,k** are easily dehydrated to the corresponding cyclic ethers (**7c-f**, **8h,i,l,n**) or lactones (**9a,c,f,k**), respectively. Finally, alcohols **6b,d,e** give, after acid treatment, the Friedel-Crafts type benzocyclopentenes **10b,d,e**.

INTRODUCTION

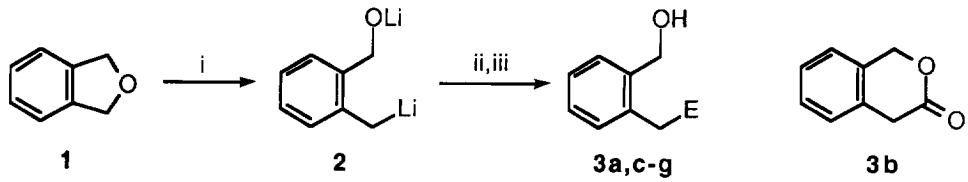
Mixed lithium/potassium dianion[1] derived from *o*-xylene **I** has been prepared[2] by double deprotonation of the corresponding arene using the Lochmann-Schlosser superbase[3]; the alkylation of this dianion afforded the expected symmetrical disubstituted compounds. Other possible routes[4a] for dianions of the type **I** involving lithiation of benzylic dihalogenides or dimesylated[4b] failed due to the almost exclusive formation of Wurtz-type products. On the other hand, we have recently described[5] that the use of a catalytic amount of an arene in the lithiation of functionalised dichlorinated precursors[6], saturated heterocycles[7] or other systems[4b,7d,8] represents a new and powerful methodology for preparing highly reactive organolithium intermediates under very mild reaction conditions. In this paper we report the di-*tert*-butylbiphenyl (DTBB)-catalysed lithiation of a simple and commercially available molecule[9,10], phthalan, and the sequential reaction of the corresponding *in situ* generated carbanionic species with electrophiles.



I

RESULTS AND DISCUSSION

The reaction of phthalan (**1**) with an excess of lithium powder (*ca.* 1:20 molar ratio) and a catalytic amount of DTBB (1:0.05 molar ratio; 2.5 mol %) in THF at ambient temperature led, after 30 min, to a solution of the dianion **2**, which reacted with different electrophilic reagents (D_2O, CO_2 and carbonyl compounds) at -78°C for 1 h yielding, after hydrolysis with water, the expected functionalised benzylic alcohols **3a-g** (Scheme 1 and Table 1). In the reaction with carbon dioxide the only product isolated after the work-up was the lactone **3b**, which resulted from the spontaneous cyclisation of the corresponding hydroxyacid initially formed (Table 1, entry 2). The same reaction shown in Scheme 1 can be carried out in absence of the catalyst: in this case the lithiation time is longer (*ca.* 5 h) and the yields are rather lower.



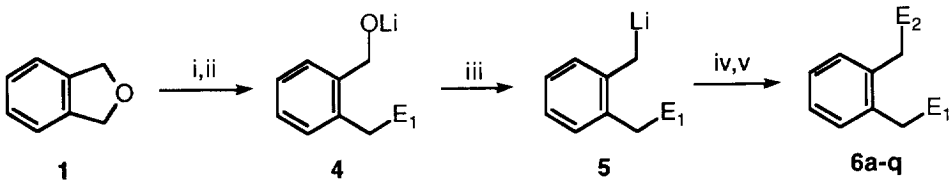
Scheme 1. *Reagents and conditions*: i, Li excess, DTBB cat. (2.5 mol %), THF, 20°C, 30 min; ii, E^+=D_2O, CO_2, Bu^tCHO, PhCHO, Et_2CO, $(CH_2)_5CO$, PhCOMe, -78°C, 1 h; iii, H_2O, -78 to 20°C.

Table 1. Preparation of Compounds **3**

Entry	Electrophile E^+	Product[a]			
		No.	E	Yield (%)[b]	R_f[c]
1	D_2O	**3a**	D	73[d]	0.18[e]
2	CO_2	**3b**	-	82	0.28[f]
3	Bu^tCHO	**3c**	Bu^tCHOH	56	0.20[f]
4	PhCHO	**3d**	PhCHOH	68	0.44[g]
5	Et_2CO	**3e**	Et_2COH	74	0.31[h]
6	$(CH_2)_5CO$	**3f**	$(CH_2)_5COH$	51	0.48[h]
7	PhCOMe	**3g**	PhC(OH)Me	63	0.51[h]

[a] All products **3** were >95% pure (GLC and 300 MHz ^1H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**. [c] Silica gel. [d] >99% deuterium from mass spectrometry and ^{13}C NMR. [e] Hexane/ethyl acetate: 5/1. [f] Hexane/ethyl acetate: 3/1. [g] Hexane/ethyl acetate: 1/1. [h] Hexane/ethyl acetate: 2/1.

The lithiation of phthalan (**1**) can be directed to the introduction of two different electrophiles at both benzylic positions in a sequential manner. Thus, once the first lithiation giving the intermediate **2** took place (Scheme 1) and this anion was allowed to react with a first electrophile E_1^+ [EtCHO, PriCHO, ButCHO, Me_2CO, Et_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, PhCH=NPh], the alcoholate **4** was obtained *in situ* (as a precursor of compounds **3**; Scheme 1); at this point the reaction mixture was stirred for four additional hours at room temperature, so a second lithiation occurred with the excess of lithium still present in the reaction media giving the new organolithium compound **5**, which finally reacted with a second electrophile E_2^+ [H_2O, D_2O, CO_2, EtCHO, ButCHO, PhCHO, Et_2CO, $(CH_2)_5CO$] at -78°C giving, after hydrolysis with water, the corresponding difunctionalised products **6a-q** (Scheme 2 and Table 2). When two molecules of a prochiral carbonyl compound were used as electrophiles E_1^+ and E_2^+ the corresponding diastereoisomers mixture was obtained in a *ca.* 1:1 molar ratio (Table 2, entry 7).



Scheme 2. *Reagents and conditions*: i, Li excess, DTBB cat. (2.5 mol %), THF, 20°C, 30 min; ii, E_1^+=EtCHO, PriCHO, ButCHO, Me_2CO, Et_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, PhCH=NPh, -78°C, 1h; iii, 20°C, 4 h; iv, E_2^+=H_2O, D_2O, CO_2, EtCHO, ButCHO, PhCHO, Et_2CO, $(CH_2)_5CO$, -78°C, 1 h; v, H_2O, -78 to 20°C.

From the products **3** and **6** prepared as shown in Scheme 1 and 2 we found specially interesting the corresponding diols **3c-g** and **6h,i,l,n** because they can act as precursors of the corresponding oxygen-containing heterocycles by a dehydration process. Thus, treatment of the mentioned diols with 85% phosphoric acid at toluene reflux[11] give the corresponding benzodihydropyrans **7c-g** and benzoxepines **8h,i,l,n**, respectively (Scheme 3 and Table 3). As it can be seen in Table 3, yields are better for the six-member than for the corresponding seven-membered heterocycles, the results being paralel to the different stability of both type of cyclic compounds[11,12].

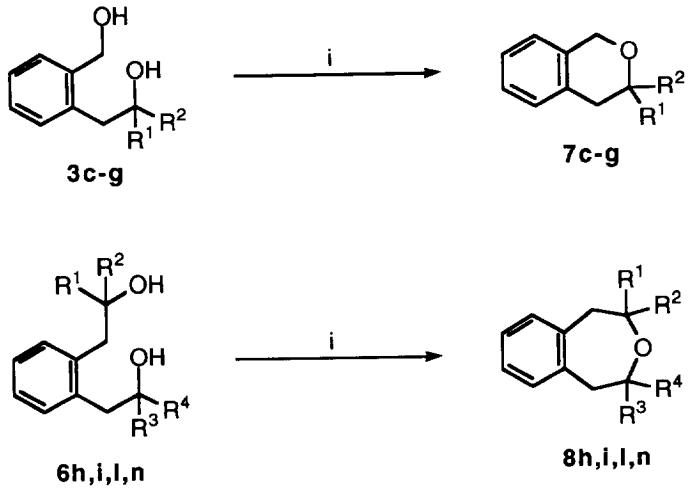
Other interesting compounds, in our opinion, are the hydroxyacids **6a,c,f,k** because their dehydration can yield seven-membered ring lactones. This was the result when the mentioned hydroxyacids were treated with a catalytic amount of *p*-toluenesulfonic acid at benzene reflux[13], so lactones **9a,c,f,k** were easily obtained (Scheme 4 and Table 4).

Table 2. Preparation of Compounds **6**

Entry	Electrophiles		Product[a]				
	E_1^+	E_2^+	No.	E_1	E_2	Yield (%)[b]	R_f[c]
1	EtCHO	CO_2	**6a**	EtCHOH	CO_2H	49	0.32[d]
2	PriCHO	H_2O	**6b**	PriCHOH	H	67	0.43[e]
3	PriCHO	CO_2	**6c**	PriCHOH	CO_2H	66	0.34[d]
4	ButCHO	H_2O	**6d**	ButCHOH	H	63	0.26[f]
5	ButCHO	D_2O	**6e**	ButCHOH	D	67[g]	0.26[f]
6	ButCHO	CO_2	**6f**	ButCHOH	CO_2H	80	0.41[d]
7	ButCHO	ButCHO	**6g**	ButCHOH	ButCHOH	61[h]	-[h,i]
8	ButCHO	$(CH_2)_5CO$	**6h**	ButCHOH	$(CH_2)_5COH$	44	0.48[j]
9	Me_2CO	EtCHO	**6i**	Me_2COH	EtCHOH	40	0.41[d]
10	Me_2CO	PhCHO	**6j**	Me_2COH	PhCHOH	34	0.51[d]
11	Et_2CO	CO_2	**6k**	Et_2COH	CO_2H	41	0.47[d]
12	Et_2CO	EtCHO	**6l**	Et_2COH	EtCHOH	41	0.21[j]
13	$(CH_2)_4CO$	H_2O	**6m**	$(CH_2)_4COH$	H	55	0.20[f]
14	$(CH_2)_4CO$	EtCHO	**6n**	$(CH_2)_4COH$	EtCHOH	38	0.48[d]
15	$(CH_2)_5CO$	Et_2CO	**6o**	$(CH_2)_5COH$	Et_2COH	39	0.50[k]
16	$(CH_2)_5CO$	$(CH_2)_5CO$	**6p**	$(CH_2)_5COH$	$(CH_2)_5COH$	26	0.28[i]
17	PhCH=NPh	D_2O	**6q**	PhCHNHPh	D	88[g]	0.27[l]

[a] All products **6** were >95% pure (GLC and 300 MHz ^1H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**. [c] Silica gel. [d] Hexane/ethyl acetate: 1/1. [e] Hexane/ethyl acetate: 5/1. [f] Hexane/ethyl acetate: 10/1. [g] >90% deuterium from mass spectrometry. [h] A diastereoisomer mixture (*ca.* 1:1, from ^1H NMR) was obtained. [i] 0.48, 0.57 (hexane/ethyl acetate: 3/1). [j] Hexane/ethyl acetate: 3/1. [k] Hexane/ethyl acetate: 2/1. [l] Hexane/ethyl acetate: 20/1.

Finally, we submitted alcohols **6b,d,e** to the same treatment as for diols **3** and **6** shown in Scheme 3. In this case a Friedel-Crafts type reaction took place leading to the indane derivatives **10b,d,e** (Scheme 5 and Table 5). From a mechanistic point of view, the first carbenium ion formed **II** suffers hydrogen or methyl 1,2-transposition to give a new more stable carbocation **III** (instead of the corresponding benzylic one), which finally undergoes S_E-type reaction yielding the obtained products **10**.

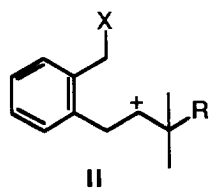


Scheme 3. *Reagents and conditions*: i, H_3PO_4, PhMe reflux, 1-10 h (see Table 3).

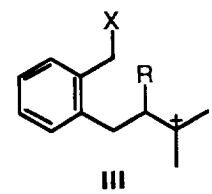
Table 3. Preparation of Compounds **7** and **8**

Entry	Starting diol	Reaction time (h)	Product[a] No	R^1	R^2	R^3	R^4	Yield (%)[b]	R_f[c]
1	**3c**	6	**7c**	H	But	-	-	82	0.45[d]
2	**3d**	2	**7d**	H	Ph	-	-	90	0.28[e]
3	**3e**	4	**7e**	Et	Et	-	-	83	0.35[e]
4	**3f**	2	**7f**	-$(CH_2)_5$-		-	-	96	0.49[e]
5	**3g**	4	**7g**	Ph	Me	-	-	94	0.29[e]
6	**6h**	10	**8h**	H	But	-$(CH_2)_5$-		68	0.49[e]
7	**6i**	1	**8i**	Me	Me	H	Et	71	0.55[f]
8	**6l**	1	**8l**	Et	Et	H	Et	52	0.23[e]
9	**6n**	1	**8n**	-$(CH_2)_4$-		H	Et	61	0.49[f]

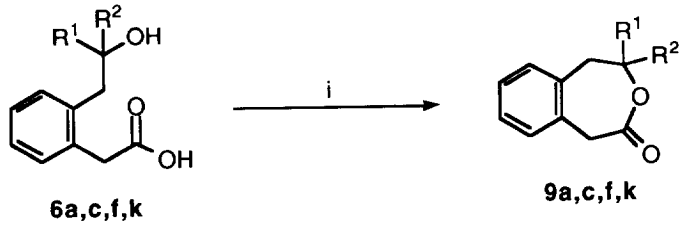
[a] All products **7** and **8** were >95% pure (GLC and 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting diol **3** or **6**. [c] Silica gel. [d] Hexane/ethyl acetate: 20/1. [e] Hexane. [f] Hexane/ethyl acetate: 10:1.



II



III



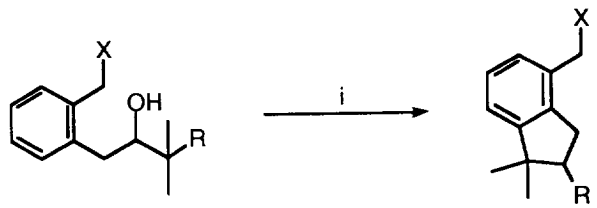
6a,c,f,k **9a,c,f,k**

Scheme 4. *Reagents and conditions*: TsOH cat., PhH reflux, 15 h.

Table 4. Preparation of Lactones **9**

Entry	Starting hydroxyacid	Product[a]				
		No.	R^1	R^2	Yield (%)[b]	R_f [c]
1	**6a**	**9a**	H	Et	73	0.35[d]
2	**6c**	**9c**	H	Pr^i	80	0.44[d]
3	**6f**	**9f**	H	Bu^t	87	0.51[d]
4	**6k**	**9k**	Et	Et	75	0.31[e]

[a] All products **9** were >95% pure (GLC and 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **6**. [c] Silica gel. [d] Hexane/ethyl acetate: 3/1. [e] Hexane/ethyl acetate: 5/1.



6b,d,e **10b,d,e**

Scheme 5. *Reagents and conditions*: i, H_3PO_4, PhMe reflux, 10h.

From the results described here we conclude that phthalan is an adequate synthon for dibenzylic dianionic derivatives of *o*-xylene; the DTBB-catalysed lithiation of this precursor followed by reaction with electrophiles yields, depending on the reaction conditions, the products of mono or disubstitution (**3** and **6**, respectively). Moreover, the obtained diols and hydroxyacids are easily dehydrated to the corresponding cyclic ethers and lactones (**7-9**), respectively.

Table 5. Preparation of Compounds **10**

Entry	Starting material	Product[a]				
		No.	X	R	Yield (%)[b]	R_f[c]
1	**6b**	**10b**	H	H	64	0.64
2	**6d**	**10d**	H	Me	92	0.64
3	**6e**	**10e**	D	Me	89	0.64

[a] All products **9** were >95% pure (GLC and 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **6**. [c] Silica gel, hexane.

EXPERIMENTAL PART

General.- For general information see reference 7e. High resolution mass spectra were performed at the corresponding service at the University of Zaragoza.

Preparation of Compounds **3**. *General Procedure.*- To a blue suspension of lithium powder (0.125 g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 20°C was added the phthalan (**1**) (0.220 ml, 2.0 mmol) under argon and the mixture was stirred for 0.5 h at the same temperature. Then, the mixture was cooled at -78°C and the corresponding electrophile (3.0 mmol; 0.5 ml in the case of water or deuterium oxide; CO_2 was bubbled for 1.5 h) was added. The mixture was stirred at the same temperature for 1 h and was hydrolysed with water. The resulting mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) and/or recrystallised to yield pure products **3a-g**. When the electrophile was CO_2, after having hydrolysed the mixture with water at -78°C it was basified with 2.5 M sodium hydroxide and extracted with ethyl acetate. The aqueous layer was then acidified with 3 M hydrochloric acid and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residue was compound **3b** [>95% pure (GLC and 300 MHz ^{1}H NMR)]. Yields and R_f values are included in Table 1; other physical, analytical and spectroscopic data follow.

(2-Deuteriomethylphenyl)methanol (**3a**): ν_{max} (film) 3700-3080 cm^{-1} (OH); δ_H 2.26 (2H, s, CH_2D), 2.50 (1H, br s, OH), 4.57 (2H, s, CH_2OH), 7.10-7.30 (4H, m, ArH); δ_C 18.2 (t, J_{CD}=19.4, CH_2D), 63.1 (CH_2OH), 125.9, 127.4, 127.5, 130.1, 135.9, 138.6 (ArC); *m/z* 123 (M+, 40%), 107 (55), 105 (100), 103 (13), 94 (33), 92 (51), 80 (11), 79 (87), 78 (33), 77 (50), 66 (22), 65 (22), 63 (21), 53 (12), 52 (22), 51 (30), 50 (22), 41 (10) (Found: M+, 123.0792. C_8H_9DO requires M, 123.0794).

1,4-Dihydro-3H-*2-benzopyran-3-one* (**3b**):[14] mp 71-72°C (pentane/dichloromethane); ν_{max} (KBr) 1740 cm^{-1} (C=O); δ_H 3.70 (2H, s, CH_2C=O), 5.30 (2H, s, CH_2O), 7.17-7.37 (4H, m, ArH); δ_C 36.1 (CH_2C=O), 70.0 (CH_2O), 124.6, 127.0, 127.3, 128.7, 13.9, 131.5 (ArC), 170.7 (C=O); *m/z* 148 (M+, 26%), 104 (100), 103 (26), 91 (29), 89 (10), 78 (31), 77 (13), 65 (16), 63 (27), 62 (11), 52 (11), 51 (33), 50 (19), 41 (10).

1-(2-Hydroxymethylphenyl)-3,3-dimethyl-2-butanol (**3c**): mp 94-95°C (pentane/dichloromethane); ν_{max} (KBr) 3700-3060 cm^{-1} (OH); δ_H 0.98 [9H, $(CH_3)_3C$], 1.25 (2H, br s, 2xOH), 2.69 (1H, dd, *J*=13.7, 10.1, Ar*H*CH), 2.78 (1H, dd, *J*=13.7, 2.6, ArHC*H*), 3.29 (1H, dd, *J*=10.1, 2.6, C*H*OH), 4.31 (1H, d, *J*=11.7, *H*CHOH), 4.73 (1H, d, *J*=11.7, HC*H*OH), 7.14-7.29 (4H, m, ArH); δ_C 25.7 [($CH_3)_3C$], 33.9 ($ArCH_2$), 35.2 [$(CH_3)_3C$], 63.2 (CH_2OH), 81.2 (CHOH), 126.4, 128.4, 130.0, 130.1, 139.4, 139.5 (ArC); *m/z* 133 [M+-$(CH_3)_3C$-H_2O, 8%), 105 (20), 104 (100), 91 (12), 77 (12), 57 (19), 41 (19). Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.95; H, 9.68. Found: C, 74.13; H, 9.82.

2-(2-Hydroxymethylphenyl)-1-phenylethanol (**3d**): mp 70-71°C (pentane/dichloromethane); ν_{max} (KBr) 3600-3080 cm^{-1} (OH); δ_H 2.95 (1H, dd, J=14.0, 3.7, *H*CHCHOH), 3.05 (1H, dd, J=14.0, 9.1, HC*H*CHOH), 3.75 (2H, br s, 2xOH), 4.37 (1H, d, J=11.8, *H*CHOH), 4.68 (1H, d, J=11.8, HC*H*OH), 4.78 (1H, dd, J=9.1, 3.7, C*H*OH), 7.14-7.36 (9H, m, ArH); δ_C 42.2 ($ArCH_2$), 63.1 (CH_2OH), 75.3 (CHOH), 125.7, 126.8, 127.5, 128.3, 128.4, 130.0, 130.5, 137.4, 139.4, 144.3 (ArC); *m/z* 210 (M^+ -H_2O, 9%), 105 (11), 104 (100), 103 (11), 77 (10). Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found : C, 79.15; H, 7.37.

2-Ethyl-1-(2-hydroxymethylphenyl)-2-butanol (**3e**)[15]: ν_{max} (film) 3600-3060 cm^{-1} (OH); δ_H 0.92 (6H, t, J=7.5, 2xCH_3), 1.44-1.60 (6H, m, 2xO*H*, 2xCH_3CH_2), 2.83 (2H, s, $ArCH_2$), 4.52 (2H, s, CH_2OH), 7.10-7.31 (4H, m, ArH); δ_C 8.0 (2xCH_3), 30.7 (2xCH_3CH_2), 40.5 ($ArCH_2$), 63.1 (CH_2OH), 74.5 (COH), 126.7, 127.5, 130.5, 131.9, 136.1, 140.3 (ArC); *m/z* 190 (M^+-H_2O, 1%), 161 (12), 105 (14), 104 (100), 91 (13), 87 (11), 77 (12), 57 (29), 45 (17), 41 (10).

1-[(2-Hydroxymethylphenyl)methyl]cyclohexanol (**3f**): mp 70-71°C (pentane/dichloromethane); ν_{max} (KBr) 3600-3060 cm^{-1} (OH); δ_H 1.19-1.61 (10H, m,5xring CH_2), 2.86 (2H, s, ArCH_2COH), 3.45 (2H, br s, 2xOH), 4.56 (2H, s, CH_2OH), 7.12-7.34 (4H, m, ArH); δ_C 22.1, 25.6, 37.9 (5xring CH_2), 44.5 ($ArCH_2$), 63.3 (CH_2OH), 71.2 (CHOH), 126.8, 127.5, 130.5, 132.1, 135.8, 140.3 (ArC); *m/z* 202 (M^+-H_2O, 9%), 105 (11), 104 (100). Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found : C, 76.10; H, 9.49.

1-(2-Hydroxymethylphenyl)-2-phenyl-2-propanol (**3g**): mp 93-94°C (pentane/dichloromethane); ν_{max} (KBr) 3600-3060 cm^{-1} (OH); δ_H 1.61 (3H, s, CH_3), 3.11 (2H, s, $ArCH_2$), 3.90 (2H, br s, 2xOH), 4.49 (2H, s, CH_2OH), 7.06-7.40 (9H, m, ArH); δ_C 29.6 (CH_3), 46.5 ($ArCH_2$), 63.1 (CH_2OH), 74.2 (COH), 125.0, 126.6, 126.8, 127.4, 128.0, 130.3, 132.0, 135.7, 139.9, 148.0 (ArC); *m/z* 224 (M^+-H_2O, 10%), 105 (18), 104 (100). Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found : C, 79.36; H, 7.78.

Preparation of Compounds **6**. *General Procedure.*- To a blue suspension of lithium powder (0.125g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 20°C was added the phthalan (**1**) (0.220 ml, 2 mmol) under argon and the mixture was stirred for 0.5 h at the same temperature. Then, the mixture was cooled at -78°C and the corresponding electrophile (3 mmol) was added. The mixture was stirred at the same temperature for 1 h and was warmed to 20°C. It was stirred at 20°C for 4 h, then it was cooled again at -78°C and a second electrophile (3 mmol; 0.5 ml in the case of water or deuterium oxide; CO_2 was bubbled for 1.5 h) was added. The mixture was stirred at -78°C for 1 h and was hydrolysed with water at the same temperature. The resulting mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The residue was then purified by column chromatography (silica gel; hexane ethyl acetate) and/or recrystallised or destilled (Kugelrohr) to yield pure products **6b**, **d**, **e**, **g-j**, **l-q**. When the electrophile was CO_2, after having hydrolysed the mixture with water at -78°C it was basified with 2.5 M sodium hydroxide and extracted with ethyl acetate. The aqueous layer was then acidified with 3 M hydrochloric acid and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residues were compounds **6a, c, f, k** [>95% pure (GLC and 300 Mhz ^{1}H NMR)]. Yields and R_f values are included in Table 2; other physical, analytical and spectroscopic data follow.

2-(2-Hydroxybutyl)phenylacetic Acid (**6a**)[15]: ν_{max} (film) 3700-2300 (COOH), 1710 cm^{-1} (C=O); δ_H 0.97 (3H, t, J=7.4, CH_3), 1.51-1.62 (2H, m, CH_3CH_2), 2.06 (2H, s, ArCH_2COOH), 2.72 (1H, dd, J=14.2, 8.7, Ar*H*CHCHOH), 2.83 (1H, dd, J=14.2, 4.1, ArHC*H*CHOH), 3.69-3.80 (1H, m, C*H*OH), 7.18-7.25 (4H, m, ArH), 7.81 (2H, br s, COOH, OH); δ_C 10.0 (CH_3), 20.7 (CH_3CH_2), 38.4, 40.0 (2x$ArCH_2$), 74.2 (CHOH), 126.8, 127.7, 130.6, 130.8, 132.6, 137.5 (ArC), 177.1 (C=O); *m/z* 190 (M^+-H_2O, 8%), 132 (29), 131 (14), 105 (16), 104 (100), 103 (14), 78 (10), 77 (12).

1-(2-Methylphenyl)-3-methyl-2-butanol (**6b**)[15]: ν_{max} (film) 3600-3100 cm^{-1} (OH); δ_H 1.01 (3H, d, J=6.8, CH_3CHCH_3), 1.02 (3H, d, J=6.8, CH_3CHCH_3), 1.52 (1H, br s, OH), 1.75-1.82 [1H, m, $(CH_3)_2CH$], 2.31 (3H, s, $ArCH_3$), 2.57 (1H, dd, J=13.7, 9.8, Ar*H*CH), 2.87 (1H, dd, J=13.7, 3.1, ArHC*H*), 3.56 (1H, ddd, J=9.8, 5.2, 3.1, C*H*OH), 7.11-7.23 (4H, m, ArH); δ_C 17.5, 18.7, 19.5 (3xCH_3), 33.5

[$(CH_3)_2CH$], 37.8 ($ArCH_2$), 76.2 (CHOH), 126.0, 126.4, 130.0, 130.4, 136.6, 137.4 (ArC); *m/z* 106 (M^+-C_4H_8O, 100%), 105 (21), 91 (51), 77 (12), 73 (23), 55 (24), 43 (32), 41 (26).

2-(2-Hydroxy-3-methylbutyl)phenylacetic Acid (**6c**)[15]:ν_{max} (film) 3800-2500 (COOH), 1770 cm^{-1} (C=O); δ_H 0.98 (6H, d, *J*=7.0, 2xCH_3), 1.73-1.84 [1H, m, $(CH_3)_2CH$], 2.66 (1H, dd, *J*=14.2, 9.7, ArHCHCHOH), 2.82 (1H, dd, *J*=14.2, 3.0, ArHCHCHOH), 3.54-3.60 (1H, m, CHOH), 3.69 (2H, s, CH_2COOH), 6.36 (2H, br s, COOH, OH), 7.16-7.24 (4H, m, ArH); δ_C 17.5, 18.6 (2xCH_3), 33.6 [$(CH_3)_2CH$], 37.0, 38.4 (2x$ArCH_2$), 77.5 (CHOH), 126.7, 127.7, 130.5, 130.8, 132.6, 138.0 (ArC), 176.6 (C=O); *m/z* 204 (M^+-H_2O, 4%), 132 (18), 115 (12), 105 (32), 104 (100), 103 (30), 78 (26), 77 (25), 51 (10), 43 (17), 41 (21).

1-(2-Methylphenyl)-3,3-dimethyl-2-butanol (**6d**)[15]:ν_{max} (film) 3600-3200 cm^{-1} (OH); δ_H 1.01 [9H, s, $(CH_3)_3C$], 1.45 (1H, br s, OH), 2.31 (3H, s, $ArCH_3$), 2.50 (1H, dd, *J*=13.7, 10.7, ArHCH), 2.92 (1H, dd, *J*=13.7, 1.9, ArHCH), 3.40 (1H, dd, *J*=10.7, 1.9, CHOH), 7.13-7.18 (4H, m, ArH); δ_C 19.6 ($ArCH_3$), 25.8 [$(CH_3)_3C$], 35.0 ($ArCH_2$), 35.4 [$(CH_3)_3C$], 79.1 (CHOH), 126.0, 126.4, 130.2, 130.5, 136.6, 137.9 (ArC); *m/z* 192 (M^+, 1%), 106 (100), 105 (34), 91 (40), 87 (18), 79 (12), 77 (16), 69 (15), 57 (22), 45 (11), 43 (12), 41 (35).

1-(2-Deuteriomethylphenyl)-3,3-dimethyl-2-butanol (**6e**)[15]: ν_{max} (film) 3680-3200 cm^{-1} (OH); δ_H 1.01 [9H, s, $(CH_3)_3C$], 1.46 (1H, br s, OH), 2.30 (2H, s, CH_2D), 2.49 (1H, dd, *J*=13.6, 10.7, ArCHH), 2.91 (1H, dd, *J*=13.6, 1.8, ArCHH), 3.40 (1H, dd, *J*=10.7, 1.8, CHOH), 7.10-7.22 (4H, m, ArH); δ_C 19.3 (t, J_{CD}=19.3, CH_2D), 25.8 [$(CH_3)_3C$], 35.0 ($ArCH_2$), 35.4 [$(CH_3)_3C$], 79.1 (CHOH), 126.0, 126.4, 130.2, 130.5, 136.6, 137.9 (ArC); *m/z* 193 (M^+, 1%), 107 (100), 106 (34), 91 (17), 87 (13), 69 (14), 57 (24), 45 (13), 43 (12), 41 (31).

2-(2-Hydroxy-3,3-dimethylbutyl)phenylacetic Acid (**6f**): mp 109-110°C (pentane/dichloromethane); ν_{max} (KBr) 3700-2380 (COOH), 1710 cm^{-1} (C=O); δ_H 0.99 (9H, s, 3xCH_3), 2.06 (2H, s, CH_2COOH), 2.61 (1H, dd, *J*=14.0, 10.7, HCHCHOH), 2.88 (1H, dd, *J*=14.0, 2.1, HCHCHOH), 3.45 (1H, dd, *J*=10.7, 2.1, CHOH), 7.18-7.25 (4H, m, ArH), 7.88 (2H, br s, COOH, OH); δ_C 25.7 [$(CH_3)_3C$], 34.7 (1x$ArCH_2$), 35.0 [$(CH_3)_3C$], 38.4 (1x$ArCH_2$), 80.6 (CHOH), 126.7, 127.7, 130.6, 130.8, 132.6, 138.5 (ArC), 177.3 (C=O); *m/z* 218 (M^+-H_2O, 5%), 133 (24), 132 (40), 105 (46), 104 (100), 103 (12), 78 (11), 77 (11), 57 (11). Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found : C, 70.91; H, 8.44.

1-[2-(2-Hydroxy-3,3-dimethylbutyl)phenyl]-3,3-dimethyl-2-butanol (**6g**) (as a *ca* 1:1 diastereoisomeric mixture). One diastereoisomer: mp 77-78°C (pentane/dichloro-methane); ν_{max} (KBr) 3680-3060 cm^{-1} (OH); δ_H 0.99 (18H, s, 6xCH_3), 2.51 (2H, br s, 2xOH), 2.71 (2H, dd, *J*=13.9, 10.4, 2xArHCH), 2.83 (2H, dd, *J*=13.9, 2.4, 2xArHCH), 3.42 (2H, dd, *J*=10.4, 2.4, 2xCHOH), 7.15-7.20 (4H, m, ArH); δ_C 25.8 (6xCH_3), 33.9 ($ArCH_2$), 35.1 [$(CH_3)_3C$], 81.2 (CHOH), 126.3, 130.0, 138.9 (ArC); *m/z* 146 (M^+-2xC_4H_9-H_2O, 1%), 87 (53), 85 (10), 69 (25), 57 (100), 55 (11), 45 (19), 43 (68), 41 (69). Anal. Calcd. for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found : C, 77.06; H, 11.00. Other diastereoisomer: mp 102-103°C (pentane/dichloro-methane); ν_{max} (KBr) 3600-3100 cm^{-1} (OH); δ_H 1.00 (18H, s, 6xCH_3), 1.52 (2H, br s, 2xOH), 2.61 (2H, dd, *J*=13.7, 10.9, 2xArHCH), 2.90 (2H, dd, *J*=13.7, 2.1, 2xArHCH), 3.47 (2H, dd, *J*=10.9, 2.1, 2xCHOH), 7.16-7.25 (4H, m, ArH); δ_C 25.9 (6xCH_3), 34.6 ($ArCH_2$), 35.0 [$(CH_3)_3C$], 79.4 (CHOH), 126.5, 130.8, 138.3 (ArC); *m/z* 185 (M^+-C_4H_9-2xH_2O, 1%), 173 (13), 133 (11), 106 (64), 105 (29), 104 (64), 91 (17), 87 (38), 69 (19), 57 (100), 45 (15), 43 (22), 41 (66). Anal. Calcd. for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found : C, 77.13; H, 11.02.

1-[2-(1-Hydroxycyclohexyl)methylphenyl]-3,3-dimethyl-2-butanol (**6h**): mp 79-80°C (pentane/dichloro-methane); ν_{max} (KBr) 3600-3080 cm^{-1} (OH); δ_H 1.00 [9H, s, $(CH_3)_3C$], 1.25 (2H, br s, 2xOH), 1.39-1.65 (10H, m, 5xring CH_2), 2.73 (1H, dd, *J*=13.9, 10.6, ArHCH), 2.77 (1H, d, *J*=13.8, HCHCOH), 2.90 (1H, d, *J*=13.8, HCHCOH), 2.97 (1H, dd, *J*=13.9, 2.0, ArHCH), 3.29 (1H, dd, *J*=10.6, 2.0, CHOH), 7.12-7.25 (4H, m, ArH); δ_C 21.9, 22.1, 25.7 (5x ring CH_2), 25.8 [$(CH_3)_3C$], 34.8 (CH_2COH), 35.1 [$(CH_3)_3C$], 37.1, 38.6 (2xring CH_2), 44.9 (CH_2COH), 71.8 (COH), 80.8 (CHOH), 125.7, 126.6, 130.2, 132.2, 136.0, 139.7 (ArC); *m/z* 233 (M^+-C_4H_9, 1%), 185 (15), 106 (35), 105 (26), 104 (46), 99 (100), 81 (30), 57 (34), 55 (17), 43 (18), 41 (33). Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found : C, 78.88; H, 10.56.

1-[2-(2-Hydroxy-2-methylpropyl)phenyl]-2-butanol (**6i**): mp 82-83°C (pentane/dichloromethane); ν_{max} (KBr) 3600-3060 cm^{-1} (OH); δ_H 0.98 (3H, t, *J*=7.4, CH_3CH_2), 1.18, 1.26 [6H, 2 s, $(CH_3)_2COH$], 1.50-1.61

(2H, m, CH_3CH_2), 2.40 (2H, br s, 2xOH), 2.79 (1H, d, J=13.9, Ar*H*CHCOH), 2.85 (2H, d, J=6.7, CH_2CHOH), 2.92 (1H, d, J=13.9, ArHC*H*COH), 3.69-3.77 (1H, m, C*H*OH), 7.14-7.21 (4H, m, ArH); δ_C 10.1 (CH_3CH_2), 29.1, 30.1 [$(CH_3)_2$COH], 39.9, 45.3 (2xArCH$_2$), 71.2 (COH), 74.3 (CHOH), 125.8, 126.6, 130.1, 132.1, 136.7, 138.5 (ArC); *m/z* 189 (M^+-H_2O-CH_3, 3%), 146 (19), 145 (14), 131 (57), 117 (100), 106 (87), 105 (26), 104 (40), 103 (11), 91 (36), 77 (11), 59 (43). Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found : C, 74.93; H, 9.21.

1-[2-(2-Hydroxy-2-phenylethyl)phenyl]-2-methyl-2-propanol (**6j**): mp 101-102°C (pentane/dichloromethane); ν_{max} (KBr) 3800-3220 cm^{-1} (OH); δ_H 1.17, 1.26 (6H, s, 2xCH_3), 2.77 (2H, br s, 2xOH), 2.72 (1H, d, J=13.9, *H*CHCOH), 2.90 (1H, d, J=13.9, HC*H*COH), 3.01 (1H, dd, J=14.0, 4.2, *H*CHCHOH), 3.19 (1H, dd, J=14.0, 9.3, HC*H*CHOH), 4.90 (1H, dd, J=9.3, 4.2, C*H*OH), 7.15-7.34 (9H, m, ArH); δ_C 29.1, 30.4 (2xCH_3), 42.5, 45.3 (2xArCH$_2$), 71.4 (COH), 75.4 (CHOH), 125.7, 126.1, 126.7, 127.4, 128.4, 130.1, 132.1, 136.7, 137.8, 144.2 (ArC); *m/z* 237 (M^+-CH_3-H_2O, 1%), 194 (16), 179 (23), 165 (31), 146 (21), 131 (33), 116 (27), 115 (11), 107 (95), 106 (49), 105 (31), 104 (15), 103 (13), 91 (34), 79 (60), 78 (18), 77 (66), 59 (100), 51 (16), 43 (47), 41 (18). Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found : C, 79.45; H, 8.13.

2-(2-Ethyl-2-hydroxybutyl)phenylacetic Acid (**6k**)[15]: ν_{max} (film) 3700-2300 (COOH), 1700 cm^{-1} (C=O); δ_H 0.92 (6H, t, J=7.4, 2xCH_3), 1.47-1.54 (4H, m, 2xCH_3CH_2), 2.83 (2H, s, ArCH_2COH), 3.84 (2H, s, CH_2COOH), 7.18-7.26 (4H, m, ArH), 8.28 (2H, br s, COOH, OH); δ_C 7.9 (2xCH_3), 30.5 (2xCH_3CH_2), 38.8, 41.1 (2xArCH$_2$), 75.8 (COH), 126.9, 127.0, 130.8, 132.2, 133.8, 135.9 (ArC), 177.7 (C=O); *m/z* 218 (M^+-H_2O, 2%), 161 (15), 145 (20), 132 (92), 117 (11), 105 (28), 104 (100), 103 (22), 91 (10), 78 (22), 77 (17), 57 (20).

2-Ethyl-1-[2-(2-hydroxybutyl)phenyl]-2-butanol (**6l**)[15]: ν_{max} (film) 3600-3080 cm^{-1} (OH); δ_H 0.87-1.01 (9H, m, 3xCH_3), 1.37-1.63 (6H, m, 3xCH_3CH_2), 2.20 (2H, br s, 2xOH), 3.71-3.77 (1H, m, C*H*OH), 7.14-7.26 (4H, m, ArH); δ_C 8.0, 10.1 (3xCH_3), 30.3, 30.4 (2xCH_3CH_2), 31.0 (CH_3CH_2CHOH), 40.0, 40.9 (2xArCH$_2$), 74.3 (CHOH), 75.1 (COH), 125.8, 126.6, 130.2, 132.1, 136.3, 138.9 (ArC); *m/z* 221 (M^+-C_2H_5, 1%), 185 (10), 146 (20), 131 (53), 117 (32), 106 (63), 105 (24), 104 (24), 91 (20), 87 (100), 57 (16), 45 (12).

1-[(2-Methylphenyl)methyl]cyclopentanel (**6m**): mp 27-28°C (pentane/dichloromethane); ν_{max} (KBr) 3600-3100 cm^{-1} (OH); δ_H 1.28 (1H, br s, OH), 1.57-1.83 (8H, m, 4xring CH_2), 2.37 (3H, s, CH_3), 2.94 (2H, s, ArCH$_2$), 7.11-7.24 (4H, m, ArH); δ_C 20.4 (CH_3), 23.2, 39.4 (4xring CH_2), 42.9 (ArCH$_2$), 83.1 (COH), 125.6, 126.4, 130.5, 131.0, 136.6, 137.3 (ArC); *m/z* 106 (M^+-C_5H_8O, 100%), 105 (24), 91 (37), 85 (37), 67 (27), 57 (12), 55 (12), 43 (13), 41 (18). Anal. Calcd. for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found : C, 81.93; H, 9.69.

1-{[2-(2-hydroxybutyl)phenyl]methyl}cyclopentanol (**6n**): mp 77-78°C (pentane/dichloromethane); ν_{max} (KBr) 3680-3080 cm^{-1} (OH); δ_H 0.99 (3H, t, J=7.5, CH_3), 1.51-1.80 (10H, m, 4xring CH_2, CH_3CH_2) 2.28 (2H, br s, 2xOH), 2.86 (2H, d, J=6.4, ArCH_2CHOH), 2.89 (1H, d, J=13.7, Ar*H*CHCOH), 3.08 (1H, d, J=13.7, ArHC*H*COH), 3.70-3.78 (1H, m, C*H*OH), 7.14-7.22 (4H, m, ArH); δ_C 10.1 (CH_3), 23.1, 23.2, 30.1, 39.2, 39.9, 40.1, 42.7, (7xCH_2), 74.3 (CHOH), 82.7 (COH), 126.0, 126.5, 130.2, 131.5, 137.3, 138.4 (ArC); *m/z* 230 (M^+-H_2O, 2%), 172 (29), 146 (25), 145 (15), 144 (10), 143 (81), 132 (10), 131 (76), 129 (20), 117 (52), 115 (15), 107 (10), 106 (100), 105 (36), 104 (53), 103 (12), 91 (40), 79 (12), 78 (10), 77 (12), 67 (21), 55 (11). Anal. Calcd. for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found : C, 77.04; H, 9.74.

1-{[2-(2-Ethyl-2-hydroxybutyl)phenyl]methyl}cyclohexanol (**6o**)[15]: ν_{max} (film) 3600-3100 cm^{-1} (OH); δ_H 0.92 (6H, t, J=7.4, 2xCH_3), 1.41-1.59 (16H, m, 5xring CH_2, 2xO*H*, 2xCH_3CH_2), 2.92 (2H, s, ArCH$_2$), 2.93 (2H, s, ArCH$_2$), 7.15-7.26 (4H, m, ArH); δ_C 8.0 (2xCH_3), 22.0, 25.8 (3xring CH_2), 30.7 (2x CH_3CH_2), 37.8 (2xring CH_2), 41.2 (ArCH$_2$), 71.9, 75.2 (2xCOH), 126.0, 126.1, 132.0, 132.1, 137.1, 137.2 (ArC); *m/z* 186 (M^+-$C_6H_{10}O$-H_2O, 20%), 185 (27), 145 (33), 117 (13), 106 (51), 105 (35), 104 (22), 99 (100), 91 (16), 87 (74), 81 (60), 80 (16), 79 (22), 77 (12), 69 (14), 57 (47), 55 (28), 45 (45), 43 (31), 41 (36).

1-{[2-(1-Hydroxycyclohexylmethyl)phenyl]methyl}cyclohexanol (**6p**): mp 101-102°C (pentane/dichloromethane); ν_{max} (KBr) 3600-3100 cm^{-1} (OH); δ_H 0.85-1.83 (22H, m, 10xring CH_2, 2xOH), 2.91 (4H, s, ArCH$_2$), 7.12-7.21 (4H, m, ArH); δ_C 21.9, 25.7, 37.6 (10xring CH_2), 45.4 (ArCH$_2$), 71.8 (2xCOH),

125.7, 132.0, 136.8 (ArC); *m/z* 186 (M^+-$C_6H_{10}O$-H_2O, 28%), 117 (10), 106 (23), 105 (31), 104 (17), 99 (100), 81 (77), 80 (19), 79 (25), 57 (11), 55 (34), 43 (21), 41 (28). Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found : C, 79.13; H, 10.81.

1-Anilino-2-(2-deuteriomethylphenyl)-1-phenylethane (**6q**): ν_{max} (film) 3380 cm^{-1} (NH); δ_H 2.19 (2H, s, CH_2D), 2.99 (1H, dd, *J*=14.2, 8.3, *H*CHCHN), 3.09 (1H, dd, *J*=14.2, 5.9, HC*H*CHN), 4.13 (1H, br s, NH), 4.56 (1H, dd, *J*=8.3, 5.9, HCHC*H*N), 6.44 (2H, dd, *J*=8.6, 1.0, *o*-ArNH), 6.61 (1H, tt, *J*=7.3, 1.0, *p*-ArNH), 7.03 (2H, dd, *J*=8.6, 7.3, *m*-ArNH), 7.06-7.33 (9H, m, ArH); δ_C 19.2 (t, J_{CD}=19.4, CH_2D), 42.6 (*C*H_2CHN), 58.2 (CHN), 113.6, 117.4, 126.0, 126.2, 126.7, 127.0, 128.5, 129.0, 129.6, 130.5, 136.0, 143.7, 147.3 (ArC); *m/z* 288 (M^+, 1%), 183 (16), 182 (100), 106 (10), 105 (10), 104 (20), 78 (12), 77 (53), 51 (13) (Found: M^+, 288.1735. $C_{21}H_{20}DN$ requires M, 288.1737).

Preparation of Compounds **7** *and* **8**. *General Procedure*.- To a solution of the corresponding diol **3c-g** or **6h**, **i**, **l**, **n** (1 mmol) in toluene (5 ml) was added 85% phosphoric acid (0.4 ml). The reaction mixture was heated at 110°C for 1-10 h, depending on the starting diol (see Table 3), then the toluene was removed by distillation and the resulting residue was hydrolysed with water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane ethyl acetate) to yield pure products **7c-g** and **8h**, **i**, **l**, **n**. Yields and R_f values are included in Table 3; other physical, analytical and spectroscopic data follow.

*3,4-Dihydro-3-(1,1-dimethylethyl)-*1H*-2-benzopyran* (**7c**): ν_{max} (film) 3020, 3000, 1570, 740 cm^{-1} (ArH); δ_H 0.99 (9H, s, 3xCH_3), 2.63 (1H, dd, *J*=16.1, 3.2, ArC*H*H), 2.81 (1H, dd, *J*=16.1, 11.4, ArCH*H*), 3.27 (1H, dd, *J*=11.4, 3.2, C*H*OH), 4.74 (1H, d, *J*=14.8, *H*CHO), 4.86 (1H, d, *J*=14.8, HC*H*O), 6.96-7.22 (4H, m, ArH); δ_C 25.8 (3xCH_3), 28.6 (*C*H_2CHO), 34.0 [$(CH_3)_3C$)], 69.0 (CHO), 82.8 (CH_2O), 124.1, 125.7, 126.2, 129.2, 134.2, 135.1 (ArC); *m/z* 175 (M^+, 1%), 133 (33), 132 (24), 105 (100), 104 (66), 103 (18), 78 (19), 77 (13), 57 (33), 51 (11), 43 (25), 41 (41) (Found: M^+, 190.1359. $C_{13}H_{18}O$ requires M, 190.1358).

*3,4-Dihydro-3-methyl-3-phenyl-*1H*-2-benzopyran* (**7d**)[16]: mp 69-70°C [lit. mp 76-77.5 (ethanol)](pentane /dichloromethane); ν_{max} (KBr) 3040, 1600, 1500, 740, 700 cm^{-1} (ArH); δ_H 2.94 (1H, dd, *J*=16.4, 3.6, *H*CHCHO), 3.06 (1H, dd, *J*=16.4, 10.6, HC*H*CHO), 4.70 (1H, dd, *J*=10.6, 3.6, CHO), 4.98 (2H, s, CH_2O), 7.00-7.45 (9H, m, ArH); δ_C 36.0 (*C*H_2CHO), 68.6 (CH_2O), 76.8 (CHO), 124.2, 125.8, 126.1, 126.4, 127.6, 128.4, 128.7, 133.4, 134.5, 142.1 (ArC); *m/z* 210 (M^+, 20%), 105 (11), 104 (100), 103 (16), 78 (15), 77 (12).

*3,3-Diethyl-3,4-dihydro-*1H*-2-benzopyran* (**7e**): ν_{max} (film) 3040, 3000, 1580, 740, 720 cm^{-1} (ArH); δ_H 0.90 (6H, s, 2xCH_3), 1.42-1.54 (2H, m, 2x*H*CHCH_3), 1.60-1.72 (1H, m, 2xHC*H*CH_3), 2.67 (2H, s, CH_2CO), 4.72 (2H, s, CH_2O), 6.96-7.15 (4H, m, ArH); δ_C 7.6 (2xCH_3), 27.5 (*C*H_2CH_3), 36.1 (*C*H_2CO), 62.5 (CH_2O), 75.1 (CO), 123.8, 125.6, 126.3, 129.2, 132.8, 134.4 (ArC); *m/z* 190 (M^+, 2%), 162 (11), 161 (100), 105 (20), 104 (52), 57 (13) (Found: M^+, 190.1359. $C_{13}H_{18}O$ requires M, 190.1358).

*Spirocyclohexane-3-[3,4-dihydro-*1H*-2-benzopyran]* (**7f**): ν_{max} (film) 3040, 1590, 740, 720 cm^{-1} (ArH); δ_H 1.35-1.76 (10H, m, 5xring CH_2), 2.66 (2H, s, CH_2CO), 4.75 (2H, s, CH_2O), 6.96-7.21 (4H, m, ArH); δ_C 21.9, 26.0, 34.8 (5xring CH_2), 38.8 (*C*H_2CO), 62.1 (CH_2O), 71.6 (CO), 123.8, 125.6, 126.2, 129.2, 132.7, 134.3 (ArC); *m/z* 202 (M^+, 25%), 184 (12), 159 (13), 142 (16), 141 (14), 131(16), 105 (11), 104 (100), 103 (11) (Found: M^+, 202.1353. $C_{14}H_{18}O$ requires M, 202.1358).

*3,4-Dihydro-3-methyl-3-phenyl-*1H*-2-benzopyran* (**7g**): ν_{max} (film) 3040, 1600, 760, 740, 700 cm^{-1} (ArH); δ_H 1.56 (3H, s, CH_3), 3.09 (1H, d, *J*=16.5, *H*CHCCH_3), 3.33 (1H, d, *J*=16.5, HC*H*CCH_3), 4.58 (1H, d, *J*=15.3, *H*CHO), 4.78 (1H, d, *J*=15.3, HC*H*O), 6.86-7.44 (9H, m, ArH); δ_C 29.8 (CH_3), 38.0 (*C*H_2C), 63.5 (CH_2O), 74.7 (CO), 123.9, 125.8, 125.9, 126.3, 126.9, 128.2, 128.5, 132.8, 134.1, 144.5 (ArC); *m/z* 224 (M^+, 11%), 105 (22), 104 (100), 103 (10), 78 (10), 77 (10) (Found: M^+, 224.1201. $C_{16}H_{16}O$ requires M, 224.1201).

Spirocyclohexane-2-[1,2,4,5-tetrahydro-4-(1,1-dimethylethyl)-3-benzoxepine] (**8h**): ν_{max} (film) 3020, 740 cm^{-1} (ArH); δ_H 0.98 (9H, s, 3xCH_3), 1.19-1.78 (10H, m, 5xring CH_2), 2.56 (1H, d, *J*=14.3, *H*CHCO),

2.75 (1H, d, J=14.3, HC*H*CO), 2.89 (1H, dd, J=14.3, 8.9, *H*CHCHO), 3.12 (1H, d, J=14.3, HC*H*CHO), 3.20 (1H, d, J=8.9, CHO), 6.96-7.22 (4H, m, ArH); δ_C 21.3, 22.4, 26.3 (3xring CH_2), 26.7 [(CH_3)$_3$C], 30.5 (CH_2CHO), 35.9 [(CH_3)$_3$*C*], 38.8, 40.7 (2x ring CH_2), 48.4 (CH_2CO), 72.9 (CHO), 77.6 (CO), 126.0, 126.4, 128.8, 130.0, 138.8, 141.1 (ArC); *m/z* 272 (M^+, 8%), 186 (23), 174 (10), 118 (17), 117 (12), 115 (10), 105 (40), 104 (100), 103 (10), 91 (10), 81 (23), 80 (17), 78 (10), 57 (46), 55 (22), 43 (16), 42 (12), 41 (56) (Found: M^+, 272.2141. $C_{19}H_{28}O$ requires M, 272.2140).

4-Ethyl-1,2,4,5-tetrahydro-2,2-dimethyl-3-benzoxepine (**8i**): ν_{max} (film) 3060, 740, 720 cm^{-1} (ArH); δ_H 0.94 (3H, t, J=7.3, CH_3CH_2), 0.99, 1.30 [6H, 2 s, (CH_3)$_2$C], 1.47-1.61 (2H, m, CH_3CH_2), 2.66 (1H, d, J=14.3, Ar*H*CHCO), 2.68 (1H, dd, J=14.9, 1.2, Ar*H*CHCHO), 2.96 (1H, dd, J=14.9, 9.3, ArHC*H*CHO), 3.16 (1H, d, J=14.3, ArHC*H*CO), 3.52-3.60 (1H, m, CHO), 6.97-7.12 (4H, m, ArH); δ_C 10.6 (CH_3CH_2), 22.9 (CH_3CCH_3), 30.6, (CH_3CH_2), 31.5 (CH_3CCH_3), 43.7 ($ArCH_2CHO$), 48.7 ($ArCH_2O$), 72.3 (CHO), 72.8 (CO), 126.0, 126.3, 129.0, 130.1, 138.6, 140.2 (ArC); *m/z* 204 (M^+, 17%), 146 (37), 132 (11), 131 (100), 117 (30), 115 (11), 104 (35), 91 (19) (Found: M^+, 204.1519. $C_{14}H_{20}O$ requires M, 204.1514).

2,2,4-Triethyl-1,2,4,5-tetrahydro-3-benzoxepine (**8l**): ν_{max} (film) 3040, 3000, 740 cm^{-1} (ArH); δ_H 0.73 (3H, t, J=7.5, CH_3CH_2CHO), 0.91, 0.93 (6H, 2 t, J=7.4, 2xCH_3CH_2CO), 1.20-1.38 (2H, m, CH_3CH_2CHO), 1.47-1.62 (4H, m, 2xCH_3CH_2CO), 2.64 (1H, dd, J=14.7, 7.0, Ar*H*CHCHO), 2.65 (1H, d, J=14.7, Ar*H*CHCO), 2.97 (1H, dd, J=14.7, 9.2, ArHC*H*CHO), 3.11 (1H, d, J=14.7, ArHC*H*CO), 3.50-3.56 (1H, m, CHO), 6.98-7.12 (4H, m, ArH); δ_C 7.2, 8.1, 10.6 (3xCH_3), 24.0, 30.8, 31.9 (3xCH_3CH_2), 43.8, 45.4 (2x$ArCH_2$), 71.2 (CHOH), 76.6 (COH), 126.0, 126.2, 128.9, 130.1, 138.5, 140.3 (ArC); *m/z* 232 (M^+, 22%), 147 (11), 146 (90), 145 (39), 131 (100), 129 (10), 115 (16), 105 (16), 104 (54), 91 (20) (Found: M^+, 232.1828. $C_{16}H_{24}O$ requires M, 232.1827).

Spirocyclopentane-2-[4-ethyl-1,2,4,5-tetrahydro-3-benzoxepine] (**8n**): ν_{max} (film) 3060, 760, 740 cm^{-1} (ArH); δ_H 0.93 (3H, t, J=7.3, CH_3), 1.20-1.86 (10H, m, 4xring CH_2, CH_3CH_2), 2.64 (1H, d, J=14.6, *H*CHCO), 2.65 (1H, dd, J=14.6, 1.2, *H*CHCHO), 3.02 (1H, dd, J=14.6, 9.1, HC*H*CHO), 3.34 (1H, d, J=14.6, HC*H*CO), 3.38-3.46 (1H, m, CHO), 6.99-7.11 (4H, m, ArH); δ_C 10.7 (CH_3), 23.0, 23.1, 30.6, 32.2, 41.6, 44.0, 46.8 (4xring CH_2, CH_3CH_2, 2x$ArCH_2$), 73.5 (CHO), 84.7 (CO), 126.0, 126.2, 128.9, 129.8, 139.2, 140.4 (ArC); *m/z* 230 (M^+, 12%), 183 (10), 173 (16), 106 (18), 105 (100), 57 (69) (Found: M^+, 230.1668. $C_{16}H_{22}O$ requires M, 230.1671).

Preparation of Compounds **9**. *General Procedure.*- A solution of the corresponding hydroxyacid **6a,c,f,k** (1mmol) in benzene (50 ml) in the presence of a catalytic amount of *p*-toluenesulfonic acid (0.001 g) was heated in a 120°C oil bath temperature at a Dean-Stark apparatus for 15 h, then the benzene was removed by distillation and the resulting residue was hydrolysed with a saturated solution of sodium carbonate and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The residue was then purified by column chromatography (silica gel; hexane ethyl acetate) and/or recrystallised to yield pure products **9a,c,f,k**. Yields and R_f values are included in Table 4; other physical, analytical and spectroscopic data follow.

4-Ethyl-4,5-dihydro-3-benzoxepin-2(1H)-one (**9a**): ν_{max} (film) 1730 cm^{-1} (C=O); δ_H 1.08 (3H, t, J=7.4, CH_3), 1.66-1.88 (2H, m, CH_3CH_2), 3.16 (2H, d, J=6.7, $ArCH_2CHO$), 3.58 (1H, d, J=14.9, *H*CHC=O), 4.44 (1H, d, J=14.9, HC*H*C=O), 4.74-4.82 (1H, m, CHO), 7.06-7.26 (4H, m, ArH); δ_C 9.8 (CH_3), 28.6 (CH_3CH_2), 39.1, 40.7 (2x$ArCH_2$), 78.0 (CHO), 126.7, 127.4, 128.7, 130.2, 130.6, 134.7 (ArC), 171.8 (C=O); *m/z* 190 (M^+, 9%), 132 (30), 131 (12), 105 (18), 104 (100), 103 (15), 78 (14) (Found: M^+, 190.0990. $C_{12}H_{14}O_2$ requires M, 190.0994).

4,5-Dihydro-4-isopropyl-3-benzoxepin-2(1H)-one (**9c**): mp 102-103°C (pentane/dichloromethane); ν_{max} (KBr) 1790 cm^{-1} (C=O); δ_H 1.07 (3H, d, J=6.9, CH_3CHCH_3), 1.08 (3H, d, J=6.9, CH_3CHCH_3), 1.95-2.05 [1H, m, C*H*(CH_3)$_2$], 3.11-3.25 (2H, m, CH_2CHO), 3.17 (1H, d, J=15.2, *H*CHC=O), 4.44 (1H, d, J=15.2, HC*H*C=O), 4.61-4.67 (1H, m, CHO), 7.06-7.26 (4H, m, ArH); δ_C 17.6, 18.5 (2xCH_3), 32.7 [*C*H(CH_3)$_2$], 36.4, 40.7 (2x$ArCH_2$), 81.2 (CHO), 126.8, 127.5, 128.8, 130.4, 130.7, 134.8 (ArC), 171.9

(C=O); *m/z* 204 (M^+, 5%), 132 (25), 115 (11), 105 (35), 104 (100), 103 (29), 78 (21), 77 (22), 43 (16), 41 (20). Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found : C, 76.35; H, 7.82.

*4-(1,1-Dimethylethyl)-4,5-dihydro-3-benzoxepin-2(*1H*)-one* (**9f**): mp 92-93°C (pentane/dichloromethane); ν_{max} (KBr) 1730 cm^{-1} (C=O); δ_H 1.07 (9H, s, 3xCH_3), 3.10-3.18 (2H, m, CH_2CHO), 3.57 (1H, d, *J*=15.2, *H*CHC=O), 4.45 (1H, d, *J*=15.2, HC*H*C=O), 4.51 (1H, dd, *J*=9.7, 3.3, CHO), 7.04-7.22 (4H, m, ArH); δ_C 25.7 (3xCH_3), 34.2 (1xArCH_2), 34.4 [(CH_3)$_3$*C*], 40.5 (1xArCH_2), 83.9 (CHO), 126.6, 127.4, 128.7, 130.5, 130.6, 134.9 (ArC), 171.8 (C=O); *m/z* 218 (M^+, 6%), 133 (22), 132 (49), 105 (40), 104 (100), 103 (17), 78 (13), 77 (13). Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found : C, 76.94; H, 8.35.

*4,4-Diethyl-4,5-dihydro-3-benzoxepin-2(*1H*)-one* (**9k**): ν_{max} (film) 1720 cm^{-1} (C=O); δ_H 0.96 (6H, t, *J*=7.4, 2x$CH_3$$CH_2$), 1.55-1.74 (4H, m, 2x$CH_3CH_2$), 3.15 (2H, s, Ar$CH_2$CO), 3.90 (2H, s, CH_2C=O), 7.14-7.25 (4H, m, ArH); δ_C 7.9 (2xCH_3), 31.3 (2xCH_3*C*H_2), 39.8 (*C*H_2C=O), 42.2 (ArCH_2CO), 88.7 (CO), 127.4, 127.7, 128.6, 129.6, 132.5, 135.2 (ArC), 169.3 (C=O); *m/z* 218 (M^+, 2%), 161 (16), 145 (19), 132 (98), 105 (15), 104 (100), 103 (14), 78 (14), 77 (10), 57 (14) (Found: M^+, 218.1313. $C_{14}H_{18}O_2$ requires M, 218.1307).

Preparation of Compounds **10**. *General Procedure.*- To a solution of the corresponding diol **6b,d,e** (1 mmol) in toluene (5 ml) was added 85% phosphoric acid (0.005 mmol, 0.4 ml). The reaction mixture was heated at 110°C for 10 h, then the toluene was removed by distillation and the resulting residue was hydrolysed with water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane ethyl acetate) to yield pure products **10b,d,e**. Yields and R_f values are included in Table 5; spectroscopic data follow.

*2,3-Dihydro-1,1,4-trimethyl-*1H*-indene* (**10b**)[17]: ν_{max} (film) 3020, 1600, 780, 760, 710 cm^{-1} (ArH); δ_H 1.25 [6H, s, (CH_3)$_2$C], 1.91 [2H, t, *J*=6.8, (CH_3)$_2$CCH_2], 2.25 (3H, s, ArCH_3), 2.80 (2H, t, *J*=6.8, ArCH_2), 6.97-7.19 (3H, m, ArH); δ_C 19.0 (ArCH_3), 28.6 [(CH_3)$_2$C*C*H_2], 28.8 [(*C*H_3)$_2$C], 40.9 (ArCH_2), 44.1 [(CH_3)$_2$*C*], 119.3, 126.6, 127.1, 133.7, 141.5, 152.3 (ArC); *m/z* 160 (M^+, 23%), 146 (14), 145 (100), 130 (12), 129 (13),128 (14), 115 (17), 105 (10), 51 (11), 41 (10).

*2,3-Dihydro-1,1,2,4-tetramethyl-*1H*-indene* (**10d**): ν_{max} (film) 3020, 1590, 780, 750, 720 cm^{-1} (ArH); δ_H 0.95 (3H, s, CH_3CCH$_3$), 1.07 (3H, d, *J*=6.9, CH_3CH), 1.27 (3H, s, CH_3CHCH_3), 2.08-2.18 (1H, m, CH_3C*H*), 2.25 (3H, s, ArCH_3), 2.41 (1H, dd, *J*=15.5, 10.1, ArC*H*H), 2.91 (1H, dd, *J*=15.5, 7.5, ArCH*H*), 6.94-7.18 (3H, m, ArH); δ_C 14.0, 19.0, 23.2, 26.7 (4xCH_3), 37.0 (ArCH_2), 45.0 (CH_3*C*H), 45.5 [(CH_3)$_2$*C*], 119.5, 126.5, 127.0, 133.5, 140.6, 153.2 (ArC); *m/z* 174 (M^+, 16%), 159 (100), 128 (17), 115 (14), 41 (14) (Found: M^+, 174.1400. $C_{13}H_{18}$ requires M, 174.1409).

*4-Deuteriomethyl-2,3-dihydro-1,1,2-trimethyl-*1H*-indene* (**10e**): ν_{max} (film) 3020, 1590, 770, 750, 710 cm^{-1} (ArH); δ_H 0.94 (3H, s, CH_3CCH$_3$), 1.06 (3H, d, *J*=6.9, CH_3CH), 1.26 (3H, s, CH_3CHCH_3), 2.07-2.15 (1H, m, CH_3C*H*), 2.22 (2H, s, ArCH_2D), 2.40 (1H, dd, *J*=15.5, 10.0, ArC*H*H), 2.91 (1H, dd, *J*=15.5, 7.6, ArCH*H*), 6.92-7.15 (3H, m, ArH); δ_C 14.0 (*C*H_3CH), 19.0 (t, J_{CD}=19.3, CH_2D), 23.2, 26.7 [(*C*H_3)$_2$C], 37.0 (ArCH_2), 45.0 (CH_3*C*H), 45.5 [(CH_3)$_2$*C*], 119.5, 126.5, 127.0, 133.4, 140.6, 153.1 (ArC); *m/z* 175 (M^+, 14%), 161 (14), 160 (100), 159 (10), 129 (15), 128 (11), 41 (14) (Found: M^+, 175.1467. $C_{13}H_{17}D$ requires M, 175.1471).

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