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Straight and versatile synthesis of substituted perhydrofuro[2,3-*b*]pyrans from 2-chloromethyl-3-(2-methoxyethoxy)propene

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Dedicated to Professor Albert I. Meyers on the occasion of his 70th birthday

Abstract—The reaction of 2-chloromethyl-3-(2-methoxyethoxy)propene with an excess of lithium powder and a catalytic amount of naphthalene (2.5%) in the presence of a carbonyl compound (E^1=R^1R^2CO) in THF at −78 to 0°C, followed by the addition of an epoxide [E^2=$R^3R^4C(O)CHR^5$] at 0 to 20°C leads, after hydrolysis, to the expected methylidenic diols. These diols when subjected to successive hydroboration–oxidation and further oxidation, spontaneous cyclization occurs to furnish a series of differently substituted perhydrofuro[2,3-*b*]pyrans.

1. Introduction

The perhydrofuro[2,3-*b*]pyran unit and related structures are present in many natural products which show interesting biological activities. Some representative members of this family of compounds are azadirachtin (**I**, isolated from the seeds of *Azadirachta indica*, with insect antifeedant and growth inhibitory activities),[1] euplotins A–C (**II**, isolated from strains of *Euplotes crassus*, which inhibit cell division or kill marine ciliates),[2] alboatrin (**III**, a phytotoxic metabolite isolated from the culture filtrate of *Verticillium alboatrum*, that causes vascular-wilt disease on alfalfa),[3] udoteatrial hydrate (**IV**, isolated from *Udotea flabellum*, with antimicrobial activity against *Staphylococcus aureus* and *Candida albicans*),[4] duroin (**V**, isolated from the roots of *Duroia hirsuta*, with allelopathic properties, which inhibits growth of other plants),[5] dimeric thymol derivatives (**VI**, isolated from *Arnica sachalinensis*),[6] norstaminol A (**VII**, a staminane-type diterperne with mild cytotoxic activity against highly liver-metastatic colon 26-L5 carcinoma cells),[7] or xyloketal A (**VIII**, an inhibitor of acetylcholine esterase isolated from a mangrove fungus of *Xylaria* species) (Chart 1).[8]

As a result of both the interesting biological activity and the structural features of these compounds, different methodologies have been settled in order to achieve the efficient construction of the perhydrofuro[2,3-*b*]pyran moiety, mainly involving radical cyclisations,[9–20] cycloadditions,[21–24] less common ring-opening processes[25] or intramolecular dehydration reactions,[26] and other cyclizations.[27] Most of these methodologies have in common the fact that they are based on intramolecular or intermolecular reactions taking place on a preformed ring. An alternative to these methods could be the preparation of acyclic dihydroxyaldehydes, as inmediate precursors of the perhydrofuropyran unit, obtained by intramolecular ketalisation. In fact, we have demonstrated that the structurally related perhydrofuro[2,3-*b*]furans can be readily obtained from the trimethylenemethane dianion synthons 3-chloro-2-(chloromethyl)propene or 2-chloromethyl-3-(2-methoxyethoxy)propene,[28] through a sequence involving arene-catalysed lithiation[29] in the presence of carbonyl compounds (Barbier-type conditions),[30] tandem hydroboration–oxidation, and final oxidation.

In order to extend this methodology to the synthesis of perhydrofuro[2,3-*b*]pyrans, we found that 2-chloromethyl-3-(2-methoxyethoxy)propene (**1**) was the substrate of choice, which by arene-catalysed selective chlorine–lithium exchange, in the presence of a carbonyl compound (the first electrophile), and subsequent allylic carbon–oxygen bond reductive cleavage followed by the addition of an epoxide (the second electrophile), led to the corresponding methylidenic diols **2**. The tandem hydroboration–oxidation of these diols, followed by final oxidation, furnished several perhydrofuropyrans **3** unsymmetrically substituted at the 2- and 6-positions (Scheme 1).[31] We want to report herein the versatility and scope of the trimethylmethylene dianion synthon **1** in the synthesis of compounds

Keywords: lithium; arene-catalysis; dianion synthons; perhydrofuropyrans.

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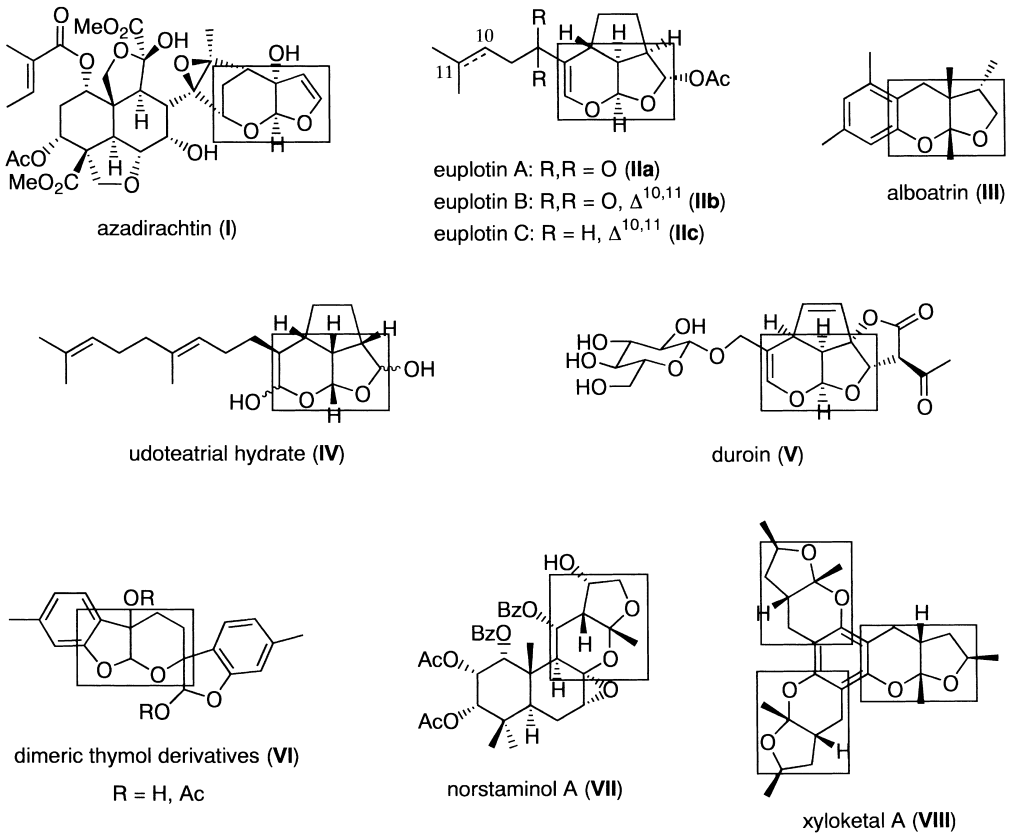
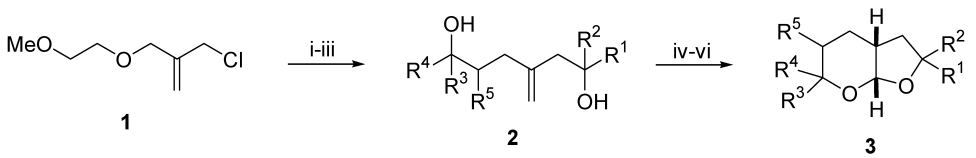


Chart 1.



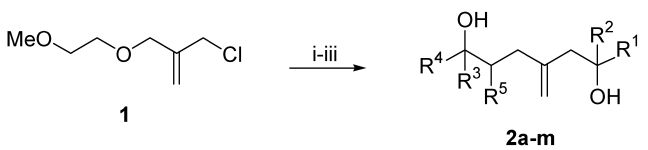
Scheme 1. *Reagents*: (i) Li, $C_{10}H_8$ (2.5%), R^1R^2CO; (ii) $R^3R^4C(O)CHR^5$; (iii) H_2O; (iv) BH_3·THF; (v) H_2O_2; (vi) PCC.

3. Thus, by proper selection of the carbonyl compound and the epoxide, not only unsymmetrically substituted, but also symmetrically substituted perhydrofuropyrans can be constructed in a straight manner. Moreover, it is also easy to obtain regioisomeric structures with the substituents at the 2- and 6-positions being exchanged.

2. Results and discussion

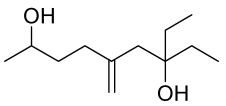
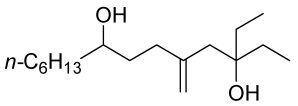
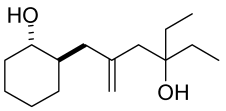
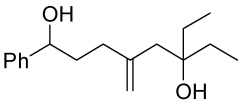
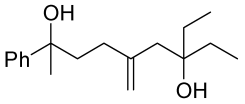
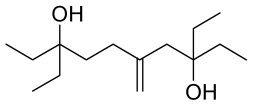
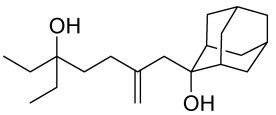
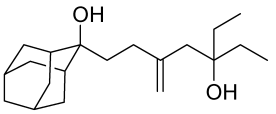
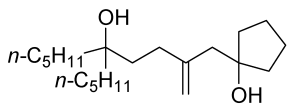
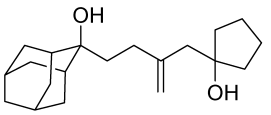
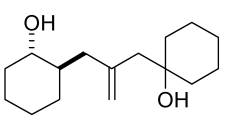
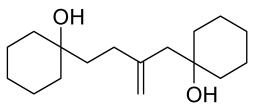
The reaction of 2-chloromethyl-3-(2-methoxyethoxy)propene (**1**) with an excess of lithium powder (1:7 molar ratio) and a catalytic amount of naphthalene (1:0.1 molar ratio, 2.5 mol%) in the presence of different carbonyl compounds (E^1=R^1R^2CO; 1:0.95 molar ratio) in THF at temperatures ranging from −78 to 0°C for ca. 3.5 h, led to a reaction mixture, which was treated with an excess of an epoxide as a second electrophile [E^2=$R^3R^4C(O)CHR^5$; 1:3 molar ratio] at 0 to 20°C overnight giving, after hydrolysis with water, the corresponding methylidenic diols **2a**–**m** (Scheme 2 and Table 1). Among them, those symmetrically substituted were readily obtained using a ketone as the first electrophile and the epoxide derived from that ketone as the second electrophile (Table 1, entries 6, 12, and 13). The versatility of the methodology was also proved in the preparation of regioisomeric structures (Table 1, entries 7 and 8). In the case of using cyclohexene oxide as the second electrophile, only the corresponding *trans*-diastereomer was obtained, its relative stereochemistry being assigned by NMR experiments[32] (Table 1, entries 3 and 11).

The reaction shown in Scheme 2 takes advantage of the different reactivity of the carbon–chlorine and carbon–oxygen bonds in arene-catalysed lithiations.[33] Thus, after



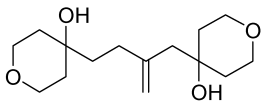
Scheme 2. *Reagents and conditions*: (i) Li, $C_{10}H_8$ cat. (2.5 mol%), E^1=R^1R^2CO, THF, −78 to 0°C; (ii) E^2=$R^3R^4C(O)CHR^5$, 0 to 20°C; (iii) H_2O.

Table 1. Preparation of unsaturated diols **2**

Entry	Ketone (E^1)		Epoxide (E^2)			Product **2**[a]		
	R^1	R^2	R^3	R^4	R^5	No.	Structure	Yields (%)[b]
1	Et	Et	H	Me	H	**2a**		54
2	Et	Et	H	n-C_6H_{13}	H	**2b**		55
3	Et	Et	H	$(CH_2)_4$		**2c**		46[c]
4	Et	Et	H	Ph	H	**2d**		68
5	Et	Et	Me	Ph	H	**2e**		31
6	Et	Et	Et	Et	H	**2f**		71
7	–[d]		Et	Et	H	**2g**		60
8	Et	Et	–[e]		H	**2h**		41
9	$(CH_2)_4$		n-C_5H_{11}	n-C_5H_{11}	H	**2i**		35
10	$(CH_2)_4$		–[e]		H	**2j**		69
11	$(CH_2)_5$		H	$(CH_2)_4$		**2k**		43[c]
12	$(CH_2)_5$		$(CH_2)_5$		H	**2l**		54

(*continued on next page*)

Table 1 (*continued*)

Entry	Ketone (E^1)		Epoxide (E^2)			Product **2**[a]		
	R^1	R^2	R^3	R^4	R^5	No.	Structure	Yields (%)[b]
13	$(CH_2)_2O(CH_2)_2$		$(CH_2)_2O(CH_2)_2$		H	**2m**		42[f]

[a] All products **2** were ≥95% pure (GLC and/or 300 MHz ^{1}H NMR) and were fully characterised by spectroscopic means (IR, ^{1}H and ^{13}C NMR, and MS).
[b] Isolated yield after column chromatography (silica gel, hexane/EtOAc) based on the starting chloroether **1**.
[c] Only the corresponding *trans*-diastereomer was obtained.
[d] Adamantan-2-one was used as the first electrophile.
[e] 2-Methylideneadamantane oxide was used as the second electrophile.
[f] Isolated yield after column chromatography (silica gel, EtOAc/MeOH) based on the starting chloroether **1**.

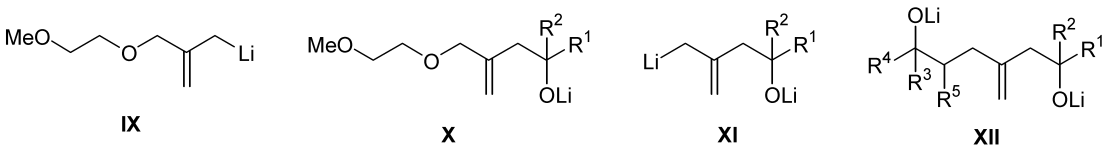


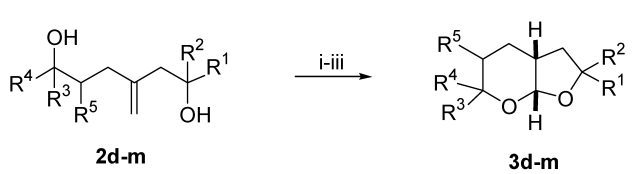
Chart 2.

the first chlorine–lithium exchange, a functionalised organolithium intermediate **IX** is formed,[34] which by reaction with a carbonyl compound (E^1) gives the expected alkoxide **X**. This species can be lithiated at higher temperatures to yield a new dilithiated compound **XI**, which by final reaction with an epoxide (E^2) affords the dialkoxide **XII**, precursor of the diol formed **2** (Chart 2).

It is worthy to note the importance of the temperature control for the reaction of intermediate **XI** with the epoxide, since the nucleophilic opening of the epoxide ring can compete with its reductive cleavage by the action of lithium. In fact, reductive cleavage mainly occurred if the epoxide was added at −78°C. On the other hand, when the epoxide addition was effected at 0°C, the product resulting from nucleophilic attack was obtained even for those epoxides which reductive cleavage is very favoured, such as styrene and α-methylstyrene oxides. Anyway, it is convenient to use an excess of the epoxide.

The transformation of diols **2** into the corresponding perhydrofuro[2,3-*b*]pyrans was carried out by conventional organic reactions (Scheme 3). Thus, successive hydroboration–oxidation with borane and hydrogen peroxide under basic conditions furnished the corresponding triols of the type **XIII** (Chart 3), which without any further purification were subjected to oxidation with PCC or $Ru(PPh_3)_3Cl_2$, giving rise to the expected products **3** (Scheme 3 and Table 2). Compounds **3** were obtained as a result of spontaneous intramolecular ketalisation of the intermediate dihydroxyaldehyde of the type **XIV** (Chart 3). When styrene or α-methylstyrene oxide were used as the second electrophiles, a ca. 1:1 diastereomeric mixture of the corresponding perhydrofuropyrans was obtained (Table 2, entries 1 and 2). For the starting diols **2d** and **2k** bearing a secondary alcohol functionality, selective oxidation of the primary alcohol functionality resulting from hydroboration–oxidation was effectively achieved with the complex $Ru(PPh_3)_3Cl_2$ (Table 2, entries 1 and 8). The *cis*-stereochemistry of the fused rings in compounds **3** was assigned unequivocally by n.O.e. experiments.

A wide range of substituents, including alkyl, aryl, and cycloalkyl fragments could be incorporated at the 2- and 6-positions of the perhydrofuro[2,3-*b*]pyran structure. Thus, by proper selection and order of the reactants, interesting symmetrically substituted (Table 2, entries 3, 9, and 10), monospirocyclic (Table 2, entries 4–6), and dispirocyclic (Table 2, entries 7, 9, and 10) derivatives were obtained. Especially, tetracyclic polyether **3m** (Table 2, entry 10) and compound **3k** (Table 2, entry 8) are very structurally attractive molecules, the latter being the only diastereomer isolated after $Ru(PPh_3)_3Cl_2$ oxidation of the precedent ca. 1:1 diastereomeric mixture of triols. The perhydrofuro[2,3-*b*]chromene skeleton of compound **3k** can be found in several norstaminane-type diterpenes such as norstaminol A (**VII**) (Chart 1).[7]



Scheme 3. *Reagents and conditions*: (i) BH_3·THF, 0°C; (ii) 33% H_2O_2, 3 M NaOH, 0°C; (iii) PCC or $Ru(PPh_3)_3Cl_2$, CH_2Cl_2, 0°C.

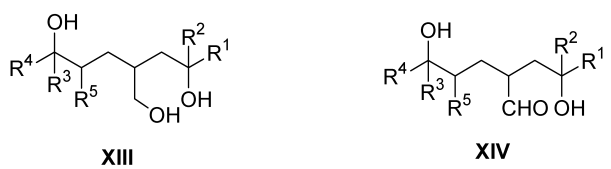
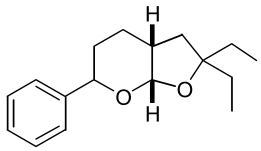
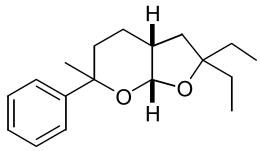
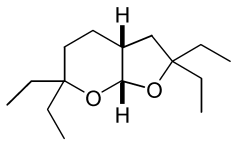
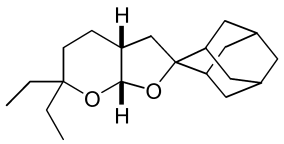
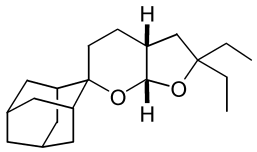
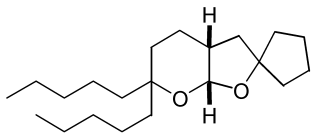
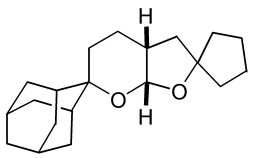
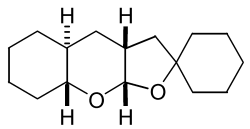
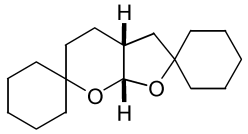
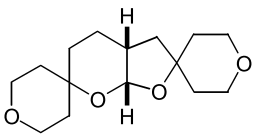


Chart 3.

Table 2. Preparation of perhydrofuropyrans **3**

Entry	Starting diol	Product **3**[a]		
		No.	Structure	Yield (%)[b]
1	**2d**	**3d**		63[c]
2	**2e**	**3e**		60[c]
3	**2f**	**3f**		73
4	**2g**	**3g**		62
5	**2h**	**3h**		57
6	**2i**	**3i**		62
7	**2j**	**3j**		64
8	**2k**	**3k**		59[d]
9	**2l**	**3l**		72
10	**2m**	**3m**		39

[a] All products **3** were ≥95% pure (GLC and/or 300 MHz ^{1}H NMR) and were fully characterised by spectroscopic means (IR, ^{1}H and ^{13}C NMR, and MS).
[b] Isolated yield after column chromatography (silica gel, hexane/EtOAc) based on the starting unsaturated diol **2**.
[c] A ca.1:1 diastereomeric mixture was obtained (GLC and 300 MHz ^{1}H NMR).
[d] This was the only compound isolated after oxidation of the precedent ca. 1:1 diastereomeric mixture of triols.

3. Conclusion

We have described herein a simple methodology which allows the straightforward preparation of differently substituted perhydrofuro[2,3-*b*]pyrans from 2-chloromethyl-3-(2-methoxyethoxy)propene, through an arene-catalysed lithiation, followed by hydroboration–oxidation, and final oxidation. The diverse electrophile combinations reacting with the organolithium intermediates makes this synthetic sequence a powerful and versatile approach to the construction of this heterocyclic moiety relatively abundant in Nature.

4. Experimental

4.1. General

Melting points were obtained with a Reichert Thermovar apparatus. NMR spectra were recorded on a Bruker AC-300 (300 MHz for H^1 NMR and 75 MHz for ^{13}C NMR) using $CDCl_3$ as solvent and TMS as internal standard; chemical shifts are given in δ (ppm) and coupling constants (J) in Hz. Mass spectra (EI) were obtained at 70 eV on a Shimadzu QP-5000 spectrometer, fragment ions in m/z with relative intensities (%) in parenthesis. HRMS analyses were carried out on a Finnigan MAT95S spectrometer. Elemental analyses were performed on a Carlo Erba CHNS-O EA1108 elemental analyser. The purity of volatile and the chromatographic analyses (GLC) were determined with a Hewlett Packard HP-5890 instrument equipped with a flame ionization detector and a 12 m capillary column (0.2 mm diameter, 0.33 mm film thickness), using nitrogen (2 ml/min) as carrier gas, $T_{injector}$=275°C, T_{column}=60°C (3 min) and 60–270°C (15°C/min); retention times (t_r) are given under these conditions. Column chromatography was performed using silica gel 60 of 40–60 microns. Thin layer chromatography was carried out on TLC plastic sheets with silica gel 60 F_{254} (Merck). THF was directly used without any purification (Acros, 99.9%) or dried over benzophenone ketyl under an argon atmosphere and distilled before use. Lithium powder was commercially available (MEDAL-CHEMY S. L.). For the preparation of 2-chloromethyl-3-(2-methoxyethoxy)propene, see Ref. 28c. Propylene, octene, styrene and cyclohexene oxides were commercially available. The other starting epoxides (α-methylstyrene, 2-pentylheptene, 2-methylideneadamantane, methylidenecyclohexane, and 4-methylideneoxacyclohexane oxides) were prepared from the corresponding ketones by reaction with the ylide derived from trimethylsulfoxonium iodide,[35] whereas 2-ethylbut-1-ene oxide was prepared by MCPBA epoxidation of the corresponding olefin.[36]

4.2. General procedure for the preparation of diols 2

A solution of 2-chloromethyl-3-(2-methoxyethoxy)propene (329 mg, 2 mmol) and the corresponding carbonyl compound (1.98 mmol) in THF (6 ml), was added for 1.5 h to a green suspension of lithium powder (100 mg, 14 mmol) and naphthalene (25 mg, 0.2 mmol) in THF (6 ml) at −78°C. The mixture was allowed to reach 0°C and then a solution of the corresponding epoxide (6 mmol) in THF (6 ml) was added for 1.5 h continuing the stirring for 8 h at room

temperature. The reaction mixture was hydrolysed with water (10 ml), extracted with ethyl acetate (3×15 ml), and the organic phase was dried over anhydrous sodium or magnesium sulfate. After removal of the solvent under reduced pressure (15 Torr), the resulting residue was purified by column chromatography (silica gel, hexane/EtOAc; EtOAc/MeOH was used for compound **2m**) to yield compounds **2**. Their physical and spectroscopic data follow.

4.2.1. 7-Ethyl-5-methylidenenonane-2,7-diol (2a). Colourless oil; t_r 10.44; R_f 0.17 (hexane/EtOAc 4:1); ν (film) 3469 (OH), 3069, 1645 (C=CH) 1100, 1054 cm^{-1} (CO); δ_H 0.86 (6H, t, J=8.0 Hz, 2×CH_3CH$_2$), 1.19 (3H, d, J=6.1 Hz, CH_3CH), 1.44 (4H, q, J=8.0 Hz, 2×CH_2CH$_3$), 1.59–1.61 (2H, m, CH_2CHCH$_3$), 1.7 (2H, br s, 2×OH), 2.15–2.28 (2H, m, CH$_2$CH_2C=C), 2.18 (2H, s, H$_2$C=CCH_2COH), 3.81 (1H, m, CH), 4.93, 4.94 (2H, 2s, H$_2$C=C); δ_C 8.0 (2×CH$_3$CH$_2$), 23.5 (CH$_3$CH), 31.1, 33.8, 37.5, 44.5 (5×CH$_2$), 67.6 (CH), 74.8 (2×COH), 113.7 (H$_2$$C$=C), 146.6 ($C$=CH$_2$); m/z 182 (M^+-18, <1%), 99 (21), 87 (91), 81 (47), 69 (18), 67 (10), 58 (20), 57 (100), 55 (29), 45 (85), 43 (49), 41 (43). HRMS calcd for $C_{12}H_{24}O_2$ 200.1776, (M^+-H_2O) 182.1671, found 182.1679.

4.2.2. 3-Ethyl-5-methylidenetetradecane-3,8-diol (2b). Colourless oil; t_r 15.79; R_f 0.12 (hexane/EtOAc 4:1); ν (film) 3389 (OH), 3080, 1643 (C=CH) 1125, 917 cm^{-1} (CO); δ_H 0.86 (6H, t, J=7.3 Hz, 2×CH_3CH$_2$CO), 0.87 (3H, t, J=4.3 Hz, CH_3(CH$_2$)$_5$), 1.07–1.69 (14H, m, (CH$_2$)$_5$, CH_2CH$_2$C=CH$_2$, 2×OH), 1.47 (4H, q, J=7.3 Hz, 2×CH_2CH$_3$), 2.04 (2H, s, H$_2$C=CCH_2COH), 2.14–2.30 (2H, m, H$_2$C=CCH_2CH$_2$), 3.52–3.67 (1H, m, CHOH), 4.93, 4.94 (2H, 2s, H$_2$C=C); δ_C 7.9, 8.0, 14.0 (3×CH$_3$), 25.6, 29.3, 30.6, 30.95, 31.8, 33.5, 35.6, 37.45, 44.5 (10×CH$_2$), 71.3 (CH), 74.8 (CH$_3$CH$_2$$C$OH), 113.47 (H$_2$$C$=C), 146.8 ($C$=CH$_2$); m/z 242 (M^+-28, <1%), 113 (10), 99 (10), 95 (22), 82 (15), 81 (58), 71 (34), 70 (35), 69 (21), 68 (47), 67 (21), 59 (16), 58 (53), 57 (20), 56 (10), 55 (83), 53 (11), 43 (100), 42 (13), 41 (70). HRMS calcd for $C_{17}H_{34}O_2$ 270.2559, ($M^+-C_2H_5$) 241.2168, found 241.2173.

4.2.3. (1*R, 2*S**)-2-[2-(2-Ethyl-2-hydroxybutyl)allyl]-cyclohexan-1-ol (2c).** Colourless oil; t_r 13.21; R_f 0.13 (hexane/EtOAc 4:1); ν (film) 3389 (OH), 3080, 1602 (C=CH), 1119, 1072, 1094 cm^{-1} (CO); δ_H 0.81, 0.83 (6H, 2t, J=8.0, 7.9 Hz, 2×CH_3CH$_2$), 1.43 (4H, 2q, J=8.0, 7.9 Hz, 2×CH_2CH$_3$), 1.56–1.99 (10H, m, (CH$_2$)$_4$, 2×OH), 1.90 (1H, dd, J=13.8, 8.3 Hz, H$_2$C=CH_AH$_B$CH), 1.92–2.00 (1H, m, CHCOH), 2.15, 2.23 (2H, AB system, J_{AB}=13.9, H$_2$C=CCH_2COH), 2.70 (1H, dd, J=13.8, 3.9 Hz, H$_2$C=CCH$_A$$H_B$CH), 3.15 (1H, m, C$H$OH), 4.76, 4.85 (2H, 2s, H$_2$C=C); δ_C 7.8, 8.2 (2×CH$_3$), 25.00, 25.7, 30.9, 31.4, 35.5, 41.3, 44.0 (8×CH$_2$), 43.4 (CHCHOH), 74.9 (CH$_3$CH$_2$$C$OH), 76.7 (CHOH), 115.3 (H$_2$$C$=C), 145.9 ($C$=CH$_2$); m/z 223 (M^+-17, 3%), 175 (11), 139 (33), 135 (11), 121 (24), 111 (11), 109 (16), 107 (18), 105 (16), 98 (32), 97 (15), 95 (20), 94 (14), 93 (34), 90 (19), 87 (32), 83 (12), 81 (70), 80 (13), 79 (35), 77 (24), 69 (22), 67 (36), 57 (81), 55 (50), 53 (22), 45 (31), 44 (41), 43 (87), 41 (100), 40 (38). HRMS calcd for $C_{15}H_{28}O_2$ 240.2089, ($M^+-C_2H_5$) 211.1698, found 211.1701.

4.2.4. 6-Ethyl-4-methylidene-1-phenyloctane-1,6-diol (2d). Colourless oil; t_r 16.32; R_f 0.11 (hexane/EtOAc 4:1); ν (film) 3410 (OH), 3090, 1602 (C=CH), 1094 cm^{-1} (CO); δ_H 0.82 (6H, t, J=7.3 Hz, 2×CH_3CH$_2$), 1.44 (4H, q, J=7.3 Hz, 2×CH_2CH$_3$), 1.75–1.90 (2H, m, CH$_2$CH_2CH, 2×OH), 1.96–2.31 (2H, m, CH_2CH$_2$CH), 2.03 (2H, s, H$_2$C=CCH_2COH), 4.64 (1H, dd, J=6.3, 4.9 Hz, CHOH), 4.91, 4.92 (2H, 2s, H$_2$C=C), 7.16–7.46 (5H, m, ArH); δ_C 7.8, 7.9 (2×CH$_3$), 30.6, 30.9, 33.6, 37.4, 44.4 (5×CH$_2$), 73.6 (CH$_3$CH$_2$$C$OH), 74.7 (CHOH), 113.6 (H$_2$$C$=C), 125.7, 127.2, 128.1, 128.2, 144.8, 144.2 (C=CH$_2$, ArC); m/z 261 (M^+-1, 3%), 146 (20), 145 (100), 143 (16), 131 (17), 128 (14), 121 (93), 120 (43), 117 (23), 115 (15), 104 (22), 103 (92), 92 (14), 91 (83), 79 (25), 78 (15), 77 (52), 73 (24), 65 (21), 63 (10), 57 (36), 51 (21), 45 (14), 44 (31), 43 (83), 42 (17), 41 (41). HRMS calcd for $C_{17}H_{26}O_2$ 262.1933, ($M^+-C_2H_5-H_2O$) 215.1436, found 215.1425.

4.2.5. 7-Ethyl-5-methylidene-2-phenylnonane-2,7-diol (2e). Colourless oil; t_r 10.05; R_f 0.27 (hexane/EtOAc 4:1); ν (film) 3389 (OH), 3053, 1596 (C=CH), 1031 cm^{-1} (CO); δ_H 0.80, 0.81 (6H, 2t, J=6.3, 7.3 Hz, 2×CH_3CH$_2$), 1.38, 1.39 (4H, 2q, J=6.3, 7.3 Hz, 2×CH_2CH$_3$), 1.56 (3H, s, CH$_3$CO), 1.57–1.77 (4H, m, CH_2CCH$_3$, 2×OH), 1.94–2.19 (4H, m, 2×CH_2C=CH$_2$), 4.75, 4.85 (2H, 2s, H$_2$C=C), 7.13–7.45 (5H, m, ArH); δ_C 8.0 (2×CH$_3$CH$_2$), 30.5 (CH$_3$COH), 30.9, 31.0, 32.2, 42.3 (5×CH$_2$), 74.7 (2×COH), 113.7, 124.8, 126.6, 128.2, 147.0 (ArC, H$_2$$C$=C), 145.8 ($C$=CH$_2$); m/z 259 (M^+-17, 6%), 105 (37), 79 (11), 44 (100), 43 (15), 42 (11). HRMS calcd for $C_{18}H_{28}O_2$ 276.2089, (M^+-2H_2O) 240.1878, found 240.1868.

4.2.6. 3,8-Diethyl-5-methylidenedecane-3,8-diol (2f). Colourless oil; t_r 11.63; R_f 0.25 (hexane/EtOAc 8:2); ν (film): 3360 (OH), 1639 (C=CH), 1027 cm^{-1} (CO); δ_H 0.83–0.96 (12H, m, 4×CH$_3$), 1.39–1.70 (14H, m, 4×CH_2CH$_3$, CH$_2$CH_2COH, 2×OH), 2.07–2.14 (4H, m, 2×CH_2C=CH$_2$), 4.80, 4.94 (2H, 2s, H$_2$C=C); δ_C 7.8, 8.1 (4×CH$_3$), 30.8, 30.9 (4×CH$_2$CH$_3$), 31.5, 36.7, 44.5 (CH$_2$CH$_2$, CH$_2$C=CH$_2$), 74.6, 74.70 (2×CO), 113.4 (H$_2$$C$=C), 147.40 ($C$=CH$_2$); m/z 206 (M^+-36, <1%), 177 (16), 138 (12), 123 (46), 109 (65), 87 (87), 83 (13), 82 (28), 81 (15), 69 (20), 67 (11), 57 (100), 55 (27). HRMS calcd for $C_{15}H_{30}O_2$ 242.2246, ($M^+-C_2H_5-2H$) 211.1698, found 211.1672.

4.2.7. 2-[2-(3-Ethyl-3-hydroxypentyl)allyl]adamantan-2-ol (2g). Colourless oil; t_r 14.98; R_f 0.28 (hexane/EtOAc 8:2); ν (film) 3403 (OH), 1636 (C=CH), 1025 cm^{-1} (CO); δ_H 0.86 (6H, t, 2×CH$_3$), 1.40–2.25 (24H, m, 10×CH$_2$, 4×CH), 2.46 (2H, *s*, 2×OH), 4.84, 4.98 (2H, 2s, H$_2$C=C); δ_C 7.8 (2×CH$_3$), 27.2, 27.3, 30.8, 31.7, 33.1, 34.6, 37.0, 37.4, 38.3, 43.6 (10×CH$_2$, 4×CH), 74.48, 74.56 (2×CO), 113.9 (H$_2$$C$=C), 147.6 ($C$=CH$_2$); m/z 288 (M^+-18, <1%), 152 (11), 151 (100), 109 (16), 57 (11). HRMS calcd for $C_{20}H_{34}O_2$ 306.2559, (M^+-H_2O) 288.2453, found 288.2550.

4.2.8. 2-[3-(2-Ethyl-2-hydroxybutyl)but-3-enyl]adamantan-2-ol (2h). Colourless oil; t_r 21.45; R_f 0.41 (hexane/EtOAc 4:1); ν (film) 3394 (OH), 3064, 1599 (C=CH), 1123, 1035 cm^{-1} (CO); δ_H 0.86 (6H, t, J=7.5 Hz, 2×CH_3CH$_2$), 1.34–1.88 (22H, m, 2×CH_2CH$_3$, CH_2CH$_2$-

C═CH_2, 5×CH_2CH, 4×CHCH_2, 2×OH), 2.18–2.25 (4H, m, 2×CH_2C═CH_2), 4.80, 4.95 (2H, 2s, H_2C═C); δ_C 8.0 (2×CH_3), 27.1, 27.2, 27.4 (4×*C*HCH_2), 32.8, 34.4, 36.5, 36.7, 38.2, 38.3, 44.2, 44.4 (10×CH_2), 113.3 (H_2*C*═C), 147.8 (C═CH_2); *m/z* 288 (M^+−18, 1%), 270 (27), 252 (18), 205 (18), 202 (57), 187 (61), 161 (10), 159 (17), 151 (29), 145 (19), 135 (82), 133 (14), 131 (18), 129 (20), 122 (28), 117 (20), 109 (18), 107 (69), 106 (13), 105 (40), 95 (16), 94 (11), 93 (62), 92 (18), 91 (74), 87 (42), 81 (39), 80 (19), 79 (13), 77 (38), 69 (21), 67 (55), 65 (16), 57 (76), 53 (25), 45 (35), 44 (13), 43 (34), 41 (100). HRMS calcd for $C_{20}H_{34}O_2$ 306.2559, (M^+−H_2O) 288.2453, found 288.2441.

4.2.9. 1-[2-(3-Hydroxy-3-pentyloctyl)allyl]cyclopentan-1-ol (2i). Colourless oil; t_r 16.43; R_f 0.37 (hexane/EtOAc 4:1); ν (film) 3395 (OH), 3055, 1612 (C═CH), 1023 cm^{-1} (CO); δ_H 0.88 (6H, t, *J*=6.1 Hz, 2×CH_3), 1.26–1.81 (28H, m, 3×$(CH_2)_4$, CH_2CH_2C═CH_2, 2×OH), 2.11 (2H, t, *J*=7.9 Hz, CH_2CH_2C═CH_2), 2.34 (2H, s, H_2C═CCH_2-COH), 4.91, 4.96 (2H, 2s, H_2C═C); δ_C 14.1 (2×CH_3), 22.6, 23.2, 23.4, 23.5, 31.2, 32.4, 37.6, 39.1, 40.0, 47.0 (15×CH_2), 75.0, 81.4 (2×COH), 116.95 (H_2*C*═C), 147.75 (C═CH_2); *m/z* 288 (M^+−36, 6%), 231 (12), 217 (32), 207 (19), 151 (11), 147 (10), 132 (42), 123 (12), 122 (12), 121 (18), 119 (13), 109 (17), 107 (17), 105 (24), 99 (16), 97 (10), 95 (35), 93 (46), 91 (30), 85 (15), 81 (50), 79 (48), 77 (18), 71 (23), 69 (37), 68 (11), 67 (59), 57 (22), 56 (10), 55 (96), 53 (16), 44 (15), 43 (86). HRMS calcd for $C_{21}H_{40}O_2$ 324.3028, (M^+−$2H_2O$) 288.2817, found 288.2825.

4.2.10. 2-[3-(1-Hydroxycyclopentylmethyl)but-3-enyl]-adamantan-2-ol (2j). Colourless oil; t_r 20.37; R_f 0.35 (hexane/EtOAc 4:1); ν (film) 3378 (OH), 3032, 1596 (C═CH), 1097, 1022 cm^{-1} (CO); δ_H 1.52–1.96 (26H, m, 5×CH_2CH, 4×CHCH_2, $(CH_2)_4$, CH_2CH_2C═CH_2, 2×OH), 2.13–2.23 (2H, m, CH_2CH_2C═CH_2), 2.36 (2H, s, H_2-C═CCH_2COH), 4.82, 4.92 (2H, 2s, H_2C═C); δ_C 23.4, 23.5, 27.4, 29.9, 32.9, 34.5, 38.3, 40.0, 47.0 (5×*C*H_2CH, *C*H_2CH_2C═CH_2, 2×*C*H_2C═CH_2, $(CH_2)_4$), 27.2, 27.3, 36.9 (4×CH), 75.0, 81.4 (2×COH), 113.05 (H_2*C*═C), 148.25 (*C*═CH_2); *m/z* 286 (M^+−18, <1%), 268 (44), 205 (20), 202 (34), 187 (46), 161 (10), 159 (13), 151 (30), 148 (11), 147 (25), 145 (18), 142 (12), 135 (24), 134 (13), 133 (87), 132 (35), 131 (24), 129 (19), 124 (41), 122 (24), 121 (12), 120 (28), 119 (25), 117 (36), 115 (11), 109 (10), 107 (28), 104 (64), 95 (14), 92 (28), 84 (21), 81 (37), 80 (22), 79 (96), 77 (43), 67 (79), 65 (18), 55 (63), 53 (29), 44 (21), 43 (33), 41 (100). HRMS calcd for $C_{20}H_{32}O_2$ 304.2402, (M^+−H_2O) 286.2297, found 286.2291.

4.2.11. (1*R, 2*S**)-1-[2-(2-Hydroxycyclohexylmethyl)-allyl]cyclohexan-1-ol (2k).** Colourless solid; t_r 14.05; R_f 0.33 (hexane/EtOAc 4:1); mp 49–51°C; ν (film) 3389 (OH), 3041, 1605 (C═CH), 1042, 916 cm^{-1} (CO); δ_H 1.30–1.82 (20H, m, $(CH_2)_5$, $(CH_2)_4$, 2×OH), 1.87 (1H, dd, *J*=13.8, 8.5 Hz, H_2C═CC$H_A$$H_B$CH), 1.92–2.00 (1H, m, C*H*COH), 2.17, 2.26 (2H, AB system, J_{AB}=13.6, H_2C═CCH_2COH), 2.70 (1H, dd, *J*=13.8, 4.1 Hz, H_2C═CC$H_A$$H_B$CH), 3.24 (1H, m, C*H*OH), 4.81, 4.91 (2H, 2s, H_2C═C); δ_C 22.3, 22.4, 24.9, 25.6, 25.8, 31.0, 35.5, 37.6, 38.3, 41.8 (11×CH_2), 43.6 (*C*HCOH), 71.6 (H_2C═CCH_2*C*OH), 75.25 (CHOH), 115.25 (H_2*C*═C), 145.8 (*C*═CH_2); *m/z* 252 (M^+, <1%), 207 (10), 105 (15), 99 (20), 98 (23), 93 (19), 91 (23), 81 (55), 80 (12), 79 (34), 77 (19), 69 (15), 67 (25), 55 (58), 53 (18), 44 (100), 43 (72), 42 (29), 41 (73). Anal. calcd for $C_{16}H_{28}O_2 \cdot 1/3H_2O$: C, 74.37; H, 11.18; found C, 74.50; H, 11.09.

4.2.12. 1-[3-(1-Hydroxycyclohexylmethyl)but-3-enyl]-cyclohexan-1-ol (2l). Colourless oil; t_r 12.21; R_f 0.32 (hexane/EtOAc 7:3); ν (film) 3366 (OH), 3068, 1637 cm^{-1} (C═CH); δ_H 1.23–1.66 (26H, m, 13×CH_2), 2.38 (2H, s, 2×OH), 4.76, 4.90 (2H, 2s, C═CH_2); δ_C 22.2, 22.5, 23.7, 29.9, 35.3, 38.5, 38.6, 39.0, 51.6 (13×CH_2), 71.2, 84.1 (2×COH), 113.3 (H_2*C*═C), 147.2 (*C*═CH_2); *m/z* 248 (M^+, <1%), 150 (30), 135 (55), 108 (13), 99 (100), 94 (29), 81 (60), 69 (17), 67 (23), 57 (11), 55 (64), 43 (41), 41 (68). HRMS calcd for $C_{17}H_{30}O_2$ 266.2246, found 266.2234.

4.2.13. 4-[3-(4-Hydroxytetrahydro-2*H*-4-pyranyl-methyl)but-3-enyl]tetrahydro-2*H*-pyran-4-ol (2m). Colourless oil; t_r 14.03; R_f 0.21 (EtOAc/MeOH 9:1); ν (film) 3406 (OH), 1640 (C═CH), 1097 cm^{-1} (CO); δ_H 1.45–1.78 (10H, m, 4×C$H_2$$CH_2O, CH_2CH_2$C═$CH_2$), 2.20–2.45 (4H, m, 2×C$H_2$C═$CH_2$), 2.47 (2H, br s, 2×OH), 3.65–3.81 (8H, m, 4×CH_2O), 4.87, 5.02 (2H, H_2C═C); δ_C 30.6, 37.6, 38.1, 38.3, 41.1 (4×*C*H_2COH, 2×*C*H_2C═CH_2, *C*H_2CH_2C═CH_2), 63.8, 63.9 (4×CH_2O), 68.8, 69.0 (2×CO), 114.4 (H_2*C*═C), 145.6 (*C*═CH_2); *m/z* 252 (M^+−18, <1%), 152 (44), 124 (50), 123 (12), 121 (12), 119 (13), 110 (11), 109 (23), 108 (28), 107 (34), 106 (15), 101 (100), 99 (12), 97 (15), 96 (85), 95 (12), 93 (28), 92 (10), 91 (17), 83 (49), 81 (13), 79 (24), 73 (19), 71 (64), 69 (12), 67 (15), 55 (33), 53 (39). HRMS calcd for $C_{15}H_{26}O_4$ 270.1831, (M^+−C_5H_9O−H_2O) 151.1123, found 151.1138.

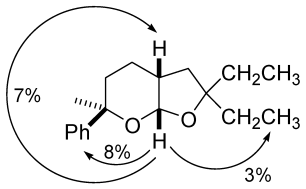
4.3. General procedures for the preparation of perhydrofuro[2,3-*b*]pyrans 3

Pyridinium chlorochromate (2.4 mmol, 517 mg) was added to a solution of the corresponding triol (1 mmol) derived from **2e**–**2j**, **2l** and **2m** in CH_2Cl_2 (5 ml) and the mixture was stirred for 6 h at room temperature. Then, it was passed through a pad containing neutral alumina, the solvent was evaporated under reduced pressure (15 Torr), and the resulting residue purified by column chromatography (silica gel, hexane/EtOAc) to yield the expected products **3e**–**3j**, **3l** and **3m**. The complex $Ru(PPh_3)_2Cl_2$ (767 mg, 0.8 mmol) was utilised instead of PCC and added to a solution of the corresponding triol (1 mmol) derived from **2d** and **2k** in benzene (10 ml). The reaction mixture was stirred for 24 h at room temperature and then passed through a pad containing neutral alumina. The solvent was evaporated under reduced pressure (15 Torr), and the resulting residue purified by column chromatography (silica gel, hexane/EtOAc) to yield the expected products **3d** and **3k**. Their physical and spectroscopic data follow.

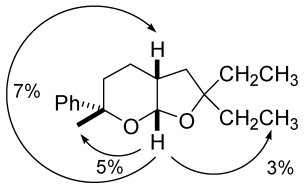
4.3.1. (3a*R, 6*R**, 7a*S**)- and (3a*R**, 6*S**, 7a*S**)-2,2-Diethyl-6-phenylperhydrofuro[2,3-*b*]pyran (3d).** Colourless oil; t_r 12.82, 13.03; R_f 0.64, 0.69 (hexane/EtOAc 8:2); ν (film) 3062, 3029 (C═CH), 1124, 1050 cm^{-1} (CO); δ_H 0.60–1.00 (12H, m, 4×CH_3), 1.20–2.00 (20H, m, 10×CH_2), 2.18, 2.32 (2H, 2m, 2×CH_2C*H*CH_2), 4.35, 4.92 (2H, 2m, 2×CH_2C*H*O), 5.14, 5.39 (2H, 2d, *J*=3.3, 4.5 Hz, 2×OCHO), 7.20–7.45 (10H, m, ArH); δ_C 8.4, 8.6, 9.0, 9.1

(4×CH_3), 23.8, 24.6, 28.5, 28.6, 30.7, 30.9, 32.1, 33.1, 35.1, 38.6 (10×CH_2), 35.4, 37.8 (2×CH_2*C*HCH_2), 71.7, 76.3 (2×CH_2*C*HO), 84.0, 88.7 (2×CH_2*C*O), 99.9, 102.3 (2×OCO), 125.7, 126.1, 127.0, 127.1, 128.2, 128.3, 142.1, 142.9 (ArC); *m/z* (t_r 12.82) 231 (M^+-29, 22%), 154 (17), 131 (14), 127 (16), 126 (100), 117 (51), 115 (12), 105 (13), 104 (49), 97 (41), 91 (32), 77 (12), 57 (39), 55 (14); *m/z* (t_r 13.03) 231 (M^+-29, 37%), 176 (11), 143 (12), 131 (24), 130 (14), 129 (13), 127 (19), 126 (74), 118 (12), 117 (85), 115 (18), 110 (20), 107 (12), 105 (24), 104 (100), 103 (13), 97 (37), 91 (50), 81 (13), 79 (11), 78 (12), 77 (17), 57 (61), 55 (19). HRMS calcd for $C_{17}H_{24}O_2$ 260.1776, (M^+-H_2O) 242.1671, found 242.1667.

4.3.2. (3a*R, 6*R**, 7a*S**) and (3a*R**, 6*S**, 7a*S**)-2,2-Diethyl-6-methyl-6-phenylperhydrofuro[2,3-*b*]pyran (3e).** Colourless oil; t_r 15.57, 15.83; R_f 0.72 (hexane/EtOAc 4:1); ν (film) 1031, 910 cm^{-1} (CO); δ_H 0.84–0.97 (12H, m, 4×C$H_3$$CH_2$), 1.39, 1.50 (6H, 2s, 2×CH_3CO), 1.44–1.93 (20H, m, 10×CH_2), 2.07–2.16, 2.31–2.37 (2H, 2m, 2×C*H*CH_2), 5.01, 5.40 (2H, 2d, *J*=3.3, 3.7 Hz, 2×OCHO), 7.19–7.49 (10H, m, ArH); δ_C 8.4, 8.5, 9.2, 9.3 (4×*C*$H_3$$CH_2$), 20.8, 20.9 (4×*C*$H_2$$CH_3$), 23.1 (2×*C*$H_3$CO), 28.2, 30.7, 30.8, 31.4, 32.9, 33.0, 34.2, 36.1 (2×$CH_2$$CH_2$, 2×*C*$H_2CCH_2$$CH_3$), 34.6, 37.4 (2×*C*HC$H_2$), 76.2, 76.6, 88.2, 88.5 (4×CH_2*C*O), 98.3, 98.6 (2×OCO), 124.2, 126.0, 126.3, 126.5, 128.0, 128.5, 149.4 (ArC); *m/z* (t_r 15.57) 274 (M^+, 5%), 245 (22), 227 (12), 145 (14), 144 (15), 131 (36), 129 (11), 127 (13), 126 (41), 121 (15), 119 (12), 118 (100), 105 (42), 103 (12), 97 (30), 91 (39), 81 (12), 79 (11), 78 (14), 77 (24), 73 (18), 57 (79), 55 (30), 53 (12), 51 (10), 43 (50), 41 (52); *m/z* (t_r 15.83) 274 (M^+, <1%), 259 (12), 245 (23), 155 (44), 145 (11), 144 (10), 139 (17), 131 (41), 129 (14), 127 (19), 126 (99), 121 (28), 119 (12), 118 (93), 117 (34), 115 (22), 109 (10), 105 (45), 103 (16), 97 (49), 95 (11), 91 (53), 81 (16), 79 (17), 77 (34), 73 (19), 69 (11), 67 (14), 57 (100), 55 (44), 53 (17), 51 (15), 44 (10), 43 (68), 41 (75). HRMS calcd for $C_{18}H_{26}O_2$ 274.1933, found 274.1929.



δ_{H3a} = 2.07–2.16, δ_{H7a} = 5.01



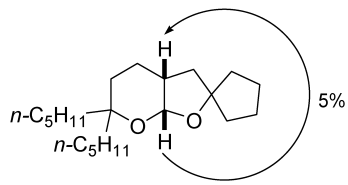
δ_{H3a} = 2.31–2.37, δ_{H7a} = 5.40

4.3.3. (3a*R, 7a*S**)-2,2,6,6-Tetraethylperhydrofuro[2,3-*b*]pyran (3f).** Colourless oil; R_f 0.71 (hexane/EtOAc 4:1); t_r 10.02; ν (film) 1122, 1017 cm^{-1} (CO); δ_H 0.75–1.00 (12H, m, 4×CH_3), 1.50–2.00 (14H, m, 7×CH_2), 2.21 (1H, m, C*H*CH_2), 5.14 (1H, d, *J*=3.3 Hz, OCHO); δ_C 7.3, 7.4, 8.3, 9.1 (4×CH_3), 19.8, 24.1, 25.2, 30.6, 31.4, 32.7, 35.8 (7×CH_2), 37.1 (*C*HCH_2), 87.5 (2×CH_2CO), 97.6 (OCO); *m/z* 239 (M^+-1, <1%), 211 (38), 175 (10), 139 (22), 126 (22), 121 (100), 111 (13), 110 (10), 97 (22), 95 (13), 84 (13), 81 (12), 69 (16), 57 (48), 55 (36). HRMS calcd for $C_{15}H_{28}O_2$ 240.2089, ($M^+-C_2H_5$) 211.1698, found 211.1672.

4.3.4. (3a*R, 7a*S**)-Spiro[adamantane-2,2′-(6′,6′-diethylperhydrofuro[2,3-*b*]pyran)] (3g).** Colourless oil; t_r 14.61; R_f 0.72 (hexane/EtOAc 8:2); mp 57–59°C; ν (film) 1135, 1090, 990 cm^{-1} (CO); δ_H 0.60–0.95 (6H, m, 2×CH_3), 1.05–2.05 (24H, m, 10×CH_2, 4×adamantyl CH), 2.07–2.30 (1H, m, C*H*CHO), 5.17 (1H, d, *J*=3.2 Hz, OCHO); δ_C 7.5, 7.7 (2×CH_3), 20.0, 24.6, 25.0, 31.5, 32.9, 34.3, 35.4, 36.4, 36.8, 37.8 (10×CH_2), 26.9, 27.0, 37.1, 37.4, 40.4 (5×*C*HCH_2), 76.8, 88.0 (2×CH_2*C*O), 97.2 (OCO); *m/z* 304 (M^+, <1%), 277 (19), 275 (100), 229 (11), 203 (29), 190 (33), 175 (14), 174 (21), 151 (39), 135 (34), 105 (11), 93 (14), 91 (20), 81 (14), 79 (21), 67 (14), 57 (23), 55 (23). Anal. calcd for $C_{20}H_{32}O_2$·1/3H_2O: C, 77.37; H, 10.60; found C, 77.38; H, 10.53.

4.3.5. (3a*R, 7a*R**)-Spiro[adamantane-2,6′-(2′,2′-diethylperhydrofuro[2,3-*b*]pyran)] (3h).** Colourless oil; t_r 16.22; R_f 0.81 (hexane/EtOAc 4:1); ν (film) 1099, 1025, 910 cm^{-1} (CO); δ_H 0.88 (6H, t, *J*=5.6 Hz, 2×C$H_3$$CH_2$), 1.25–1.95 (24H, m, 2×C$H_2$$CH_3$, 7×C*H*$_2CH, CH_2$$CH_2$CH, 4× adamantyl CH), 2.01–2.22 (1H, m, C*H*CHO), 5.17 (1H, d, *J*=3.7 Hz, OCHO); δ_C 8.5, 8.9 (2×CH_3), 14.2, 19.9 (2×*C*$H_2$$CH_3$), 27.6, 27.8, 29.8, 30.9, 39.6 (5×C*H*CH_2), 29.7, 31.4, 32.0, 32.5, 32.6, 34.0, 34.1, 35.8 (5×*C*H_2CH, *C*H_2*C*H_2, *C*H_2CC$H_2$$CH_3$), 87.6, 96.8 (2×$CH_2$CO), 96.8 (OCO); *m/z* 304 (M^+, <1%), 275 (34), 161 (17), 126 (100), 110 (15), 105 (13), 97 (24), 95 (15), 93 (15), 92 (12), 91 (22), 81 (21), 79 (29), 77 (12), 69 (10), 67 (23), 57 (57), 55 (43), 53 (12), 44 (12), 43 (29), 41 (59), 40 (15). HRMS calcd for $C_{20}H_{32}O_2$ 304.2402, found 304.2391.

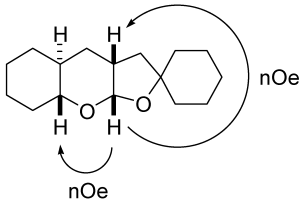
4.3.6. (3a*R, 7a*S**)-Spiro[cyclopentane-1,2′-(6′,6′-dipentylperhydrofuro[2,3-*b*]pyran)] (3i).** Colourless oil; t_r 15.98; R_f 0.85 (hexane/EtOAc 4:1); ν (film) 1105, 1018, 904 cm^{-1} (CO); δ_H 0.88 (6H, t, *J*=5.6 Hz, 2×C$H_3$$CH_2$), 1.16–2.17 (30H, m, 15×CH_2), 2.10–2.21 (1H, m, C*H*CH_2), 5.12 (1H, d, *J*=3.8 Hz, OCHO); δ_C 14.1 (2×CH_3), 22.6, 22.7, 22.9, 23.5, 23.8, 26.5, 32.5, 32.6, 32.7, 37.5, 39.7, 39.9 (15×CH_2), 37.8 (*C*HCH_2), 76.7, 77.2 (2×CH_2*C*O), 97.6 (OCO); *m/z* 322 (M^+-29, <1%), 251 (58), 233 (18), 215 (17), 151 (14), 137 (27), 124 (59), 119 (27), 109 (14), 108 (15), 99 (18), 97 (13), 95 (30), 93 (16), 91 (11), 85 (12), 83 (17), 81 (36), 79 (22), 71 (21), 69 (31), 67 (46), 56 (27), 55 (95), 53 (11), 43 (97), 41 (100), 40 (10). HRMS calcd for $C_{21}H_{38}O_2$ 322.2872, found 322.2890.



4.3.7. (3a*R, 7a*R**)-Dispiro[adamantane-2,6′-perhydrofuro[2,3-*b*]pyran-2′,1″-cyclopentane] (3j).** Colourless oil; t_r 16.82; R_f 0.76 (hexane/EtOAc 4:1); ν (film) 1112, 1042 cm^{-1} (CO); δ_H 1.23–1.99 (28H, m, 12×CH_2, 4× adamantyl CH), 2.07–2.25 (1H, m, C*H*CHO), 5.16 (1H, d, *J*=3.7 Hz, OCHO); δ_C 21.1, 23.7, 26.1, 29.7, 32.0, 32.5, 34.0, 34.2, 38.0, 39.3, 40.1, 40.4 (12×CH_2), 27.6, 27.8, 30.2, 38.1, 38.4 (4×adamantyl CH, *C*HCHO), 92.1 (2×CH_2*C*O), 96.8 (OCO); *m/z* 303 (M^++1, 2%), 302 (M^+, 7%), 202 (14), 161 (25), 149 (21), 148 (100), 135 (11), 133 (11), 119 (13), 108 (22), 107 (13), 105 (16), 95 (14), 93 (25), 92 (17), 91 (33), 81 (24), 79 (42), 77 (16), 67 (36), 55 (37), 53 (13), 43

(13), 41 (50). HRMS calcd for $C_{20}H_{30}O_2$ 302.2246, found 302.2238.

4.3.8. (3a*R, 4a*S**, 8a*R**, 9a*S**)-Spiro[cyclohexane-1,2′-perhydrofuro[2,3-*b*]chromene] (3k).** Colourless oil; t_r 12.59; R_f 0.73 (hexane/EtOAc 8:2); ν (film) 1076 cm^{-1} (CO); δ_H 1.10–1.80 (23H, m, 11×CH_2, $CH_2CH_2CHCH_2$), 2.31 (1H, m, $CHCH_2C$), 2.88 (1H, m, CH_2CHO), 4.98 (1H, d, J=3.4 Hz, OCHO); δ_C 24.8, 25.5, 25.8, 31.0, 31.4, 32.3, 37.0, 37.8, 40.5 (11×CH_2), 35.5 ($CH_2CH_2CHCH_2$), 38.8 (CCH_2CHCH_2O), 77.2, 85.4 (CH_2CHO, CH_2CO) 101.4 (OCO); *m*/*z* 250 (M^+, 56%), 207 (36), 152 (32), 151 (26), 139 (15), 138 (100), 137 (13), 135 (18), 133 (15), 122 (53), 121 (18), 120 (11), 119 (29), 95 (28), 94 (27), 91 (18), 82 (15), 81 (42), 80 (13), 79 (35), 69 (12), 67 (48), 57 (10), 55 (48), 54 (10), 53 (14). HRMS calcd for $C_{16}H_{26}O_2$ 250.1933, found 250.1949.



(NOESY)

4.3.9. (3a*R, 7a*S**)-Dispiro[cyclohexane-1,2′-perhydrofuro[2,3-*b*]pyran-6′,1″-cyclohexane] (3l).** Colourless oil; t_r 12.59; R_f 0.50 (hexane/EtOAc 9:1); ν (film) 1012, 990 cm^{-1} (CO); δ_H 1.21–1.75 (22H, m, 2×$(CH_2)_5$, CH_2CH_2CH), 1.90–2.03 (4H, m, CH_2CHCH_2), 2.18–2.33 (1H, m, $CHCH_2$), 5.16 (1H, d, J=3.7 Hz, OCHO); δ_C 19.9, 21.6, 24.1, 24.3, 25.9, 26.1, 28.8, 29.7, 30.7, 38.0, 39.4, 40.5 (13×CH_2), 37.3, (CH_2CHCH_2), 73.6, 84.5 (2×CH_2CO) 97.0 (OCO); *m*/*z* 264 (M^+, 28%), 122 (27), 177 (17), 151 (74), 138 (41), 132 (36), 99 (15), 81 (49), 67 (56), 55 (81), 43 (35), 41 (100). HRMS calcd for $C_{17}H_{28}O_2$ 264.2089, found 264.2088.

4.3.10. (3a*R, 7a*S**)-Dispiro[(1-oxacyclohexane)-4,2′-perhydrofuro[2,3-*b*]pyran-6′,4″-(1″-oxacyclohexane)] (3m).** Colourless oil; R_f 0.56 (EtOAc/MeOH); t_r 13.41; ν (film) 1111, 1039 cm^{-1} (CO); δ_H 1.05–1.92 (14H, m, 4×CH_2CH_2O, $CH_2CH_2CHCH_2$), 2.12 (1H, m, $CHCH_2$), 3.75–3.90 (8H, m, 4×CH_2O), 5.19 (1H, d, J=3.3 Hz, OCHO); δ_C 30.7, 37.6, 38.0, 38.1, 38.4, 38.7 (7×CH_2, $CHCH_2$), 64.0, 64.1 (4×CH_2O), 78.5, 87.9 (2×CH_2CO), 101.8 (OCO); *m*/*z* 268 (M^+, <1%), 250 (10), 219 (13), 198 (35), 151 (50), 138 (15), 137 (100), 132 (19), 121 (88), 95 (18), 91 (28), 79 (38), 69 (24), 67 (47), 55 (31). HRMS calcd for $C_{15}H_{24}O_4$ 268.1675, (M^+-H_2O) 250.1568, found 250.1591.

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