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New Trimethylenemethane Dianion Synthons: Application to the Preparation of Substituted Perhydrofuro[2,3-*b*]furans

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Abstract—The reaction of 3-chloro-2-(chloromethyl)prop-1-ene (**1**) with lithium powder and a catalytic amount of naphthalene in the presence of different electrophiles in THF at −78°C yields products **2**. When carbonylic compounds are used as electrophiles the corresponding methylenic diols are obtained, which by tandem hydroboration–oxidation with alkaline hydrogen peroxide and treatment with PCC (for ketone derivatives) or $(Ph_3P)_3RuCl_2$ (for aldehyde derivatives) furnish the expected perhydrofurofurans **3**. Using 2-chloromethyl-3-(2-methoxyethoxy)prop-1-ene (**4**) as starting material and under the above conditions, the selective chloro/lithium exchange versus the allylic carbon–oxygen bond cleavage allows the introduction of a first electrophile at −78 to −30°C, and a second electrophile at −30°C to room temperature to give products **5**. The same oxidation protocol mentioned above, when applied to diols **5**, lead to the differently substituted perhydrofurofurans **7**. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

The perhydrofurofuran unit is present in many biologically active natural products. One important family of molecules having this fragment belong to the clerodan-type diterpenes, which show potential insect antifeedant activity[1] as well as antibacterial activity.[2] Some representative examples are lupulin A, scuterepenin A_1[3] or scupolin B (Fig. 1).[4] In some cases, the mentioned heterocyclic core is attached to a steroid structure, such as in the case of vernionioside D_1.[5] However, aflatoxin B_2[6,7] and asteltoxin[8] are, probably, the most famous members of the perhydrofurofuran core-containing molecules because they are important mycotoxins with very potent toxicity and carcinogenecity,[9] and they have been detected in several foods, therefore intense interest from toxicologists and government regulators has been shown.[10]

Most of the methodologies to synthesise the 1,7-dioxabicyclo[3.3.0]octane moiety use an inter- or intramolecular cylisation on a preformed tetrahydrofuran ring through dehydration,[11] radical cyclisation,[12] iodocycloetherification,[13] dipolar cycloaddition,[14] intramolecular carbozincation,[15] intramolecular carbenoid insertion[16] or metal-promoted cyclisation,[17] among others. Ten years ago, de Groot et al.[18a] reported the synthesis of perhydrofurofuran **II** starting from the di-*O*-silylated dihydroxyaldehyde **I** by acid-catalysed cyclisation in 20% yield (Scheme 1). This double cyclisation prompted us to use a different strategy from an analogue of compound **I** using a trimethylenemethane synthon **III** and a carbonyl compound **IV** to build the carbon skeleton corresponding to the bicycle **II**. Dianion **III**, which has interest not only from a theoretical[19] but also from a synthetic point of view (two electrophilic fragments can be introduced in only one step), can be prepared by double deprotonation using *n*-butyllithium in the presence of tetramethylethylenediamine (TMEDA),[20] or potassium *tert*-butoxide.[21,22] However, the use of a chloro/lithium exchange reaction for the preparation of **III** failed due to the intermolecular coupling of the monolithium derivative initially formed. This problem was overcome recently[23] using an arene-catalysed lithiation[20–26] in the presence of several carbonyl compounds (Barbier type conditions).[27] In this paper we apply this methodology[28] to generate dianions[28c] of the type **III** as the key step in the synthesis of the perhydrofurofuran core of compounds of the type shown in Fig. 1.[29]

Results and Discussion

The reaction of 3-chloro-2-(chloromethyl)prop-1-ene (1)[30] with lithium and a catalytic amount of naphthalene (5 mol%) in the presence of different electrophiles [Pr^iCHO, Bu^tCHO, Me_2CO, Et_2CO, Cy_2CO, $(CH_2)_5CO$, $Y(CH_2CH_2)_2CO$ (Y=O, S, Pr^nN), Bu^tCOMe, PhCOMe, EtCOMe, Me_3SiCl, $(MeS)_2$] in THF at temperatures ranging from −78 to 20°C led, after hydrolysis with water, to the expected compounds **2** (Scheme 2 and Table 1), some of them (compounds **2a**, **2c**, **2d**, and **2f**, Table 1, entries 1, 3, 4, and 6, respectively) having been already described by us using the same methodology.[23]

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

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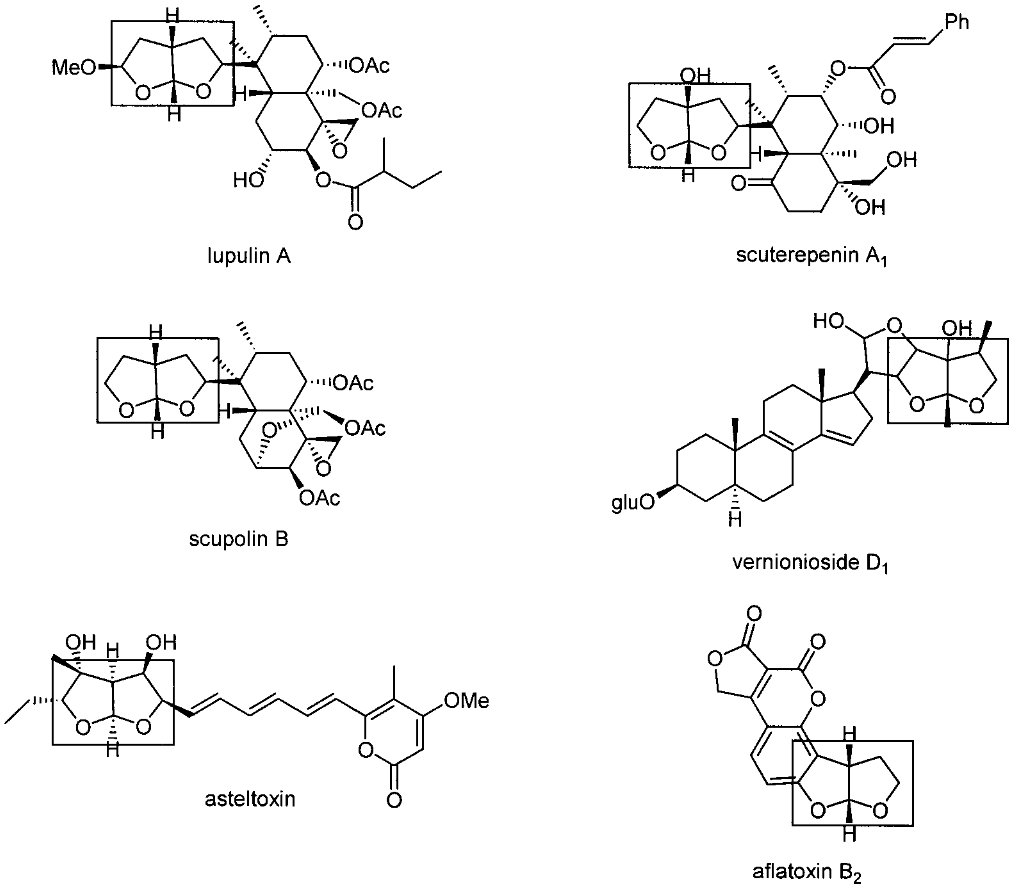
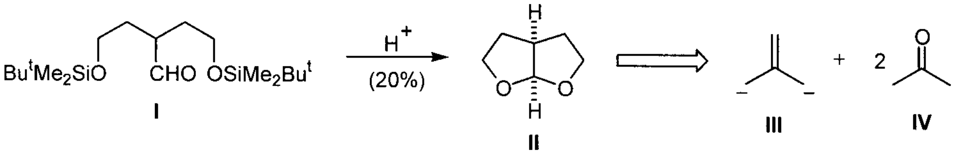


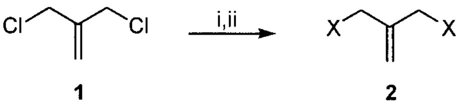
Figure 1.



Scheme 1.

Concerning the mechanism of this reaction, we think that the reaction involves a double tandem process of lithiation–S_E reaction with the electrophile present in the reaction medium. In the absence of the electrophile, an intramolecular coupling of the monolithium intermediate initially formed takes place, giving 1,4-dimethylenecyclohexane as the only reaction product.[25] For these reactions, we think that a dilithiated species, corresponding to the dianion **III**, is probably not generated.

The transformation of the unsaturated diols **2** derived from carbonyl compounds into the corresponding perhydrofurofurans **3**, was carried out in a three-step process involving first a hydroboration with borane in THF at 0°C, followed by in situ oxidation with 33% hydrogen peroxide in 3 M sodium hydroxide at 0°C. The resulting triol intermediates were not purified and were further oxidised using two different methods depending on the nature of the triol: dichlorotris(triphenylphosphine)ruthenium(II) in benzene at 0°C (Method A, for R^2=H) or pyridinium chlorochromate (PCC) in CH_2Cl_2 at 0°C (Method B, for $R^2 \neq H$) (Scheme 3 and Table 2).



Scheme 2. Reagents and conditions: (i) Li, $C_{10}H_8$ cat. (5%), E=Pr^{i}CHO, Bu^{t}CHO, Me_2CO, Et_2CO, Cy_2CO, $(CH_2)_5CO$, $Y(CH_2CH_2)_2CO$ (Y=O, S, Pr^{n}N), Bu^{t}COMe, PhCOMe, EtCOMe, Me_3SiCl, $(MeS)_2$, THF, −78 to 20°C; (ii) H_2O.

In the transformation **2**→**3**, non-isolated compounds of the type **V**–**VII** are probably involved, the last one undergoing spontaneous cyclisation to give directly the expected products **3** (Fig. 2).

In the case of aldehyde (**3a**, **b**) or unsymmetrically substituted ketone (**3j**, **k**) derivatives (Table 2, entries 1, 2, 8, and 9, respectively), the expected mixture of diastereoisomers (*trans*+α-*cis*+β-*cis*) was obtained (Fig. 3), which could be separated by column chromatography (except for

Table 1. Preparation of compounds **2**

Entry	Electrophile	Product[a]		
		No.	X	Yield (%)[b]
1	Pr^iCHO	**2a**	Pr^iCHOH	64[c]
2	Bu^tCHO	**2b**	Bu^tCHOH	61[c]
3	Me_2CO	**2c**	Me_2COH	74
4	Et_2CO	**2d**	Et_2COH	72
5	Cy_2CO[d]	**2e**	Cy_2COH	50
6	$(CH_2)_5CO$	**2f**	$(CH_2)_5COH$	67
7	$O(CH_2CH_2)_2CO$	**2g**	$O(CH_2CH_2)_2$	56
8	$S(CH_2CH_2)_2CO$	**2h**	$S(CH_2CH_2)_2COH$	43
9	$Pr^nN(CH_2CH_2)_2CO$	**2i**	$Pr^nN(CH_2CH_2)_2COH$	34
10	Bu^tCOMe	**2j**	$Bu^tC(OH)Me$	66[c]
11	PhCOMe	**2k**	PhC(OH)Me	41[c]
12	EtCOMe	**2l**	EtC(OH)Me	52[c]
13	Me_3SiCl	**2m**	Me_3Si	73[e]
14	$(MeS)_2$	**2n**	MeS	82[e]

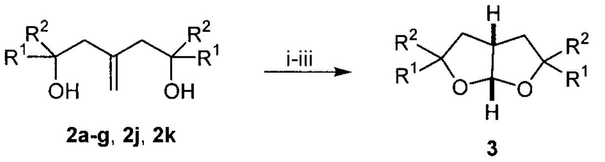
[a] All products **2** were >95% pure (GLC and 300 MHz ^1H NMR) and were fully characterised by spectroscopic means (IR, ^1H and ^{13}C NMR, and mass spectrometry).

[b] Isolated yield after column chromatography (silica gel, hexane/diethyl ether) based on the starting material **1**, unless otherwise is stated.

[c] Product **2** was obtained as a ca. 1:1 mixture of diastereoisomers.

[d] Cy=cyclohexyl.

[e] Crude reaction yield.



Scheme 3. Reagents and conditions: (i) $BH_3 \cdot THF$, 0°C; (ii) 33% H_2O_2, 3 M NaOH, 0°C; (iii) $(Ph_3P)_3RuCl_2$, PhH, 0°C (for R^2=H) or PCC, CH_2Cl_2, 0°C.

compound **3k**) and their structures unequivocally assigned by 300 or 500 MHz ^1H NMR analysis (see Experimental).

In the second part of this study we have introduced the reagent 2-chloromethyl-3-(2-methoxyethoxy)prop-1-ene (**4**) in order to be able to prepare perhydrofurofurans resulting from the introduction of two different carbonyl compounds. Thus, using different reaction temperatures it was possible to perform the chloro/lithium exchange at −78°C, introducing the first electrophile (Barbier conditions), whereas after warming up to −30°C the allylic carbon–oxygen bond reductive cleavage took place allowing the introduction of the second electrophile. After hydrolysis with water, compounds **5** were isolated (Scheme 4 and Table 3).

As Table 3 shows, a variety of electrophiles (E^1 and E^2) can be used in both steps, making the reaction very versatile compared to other similar processes working under Barbier-type conditions. It is noteworthy that halogenated materials can be used as electrophiles under the mentioned conditions, this reaction being rare using reactive functionalised organolithium intermediates.[25,27,28]

Concerning a mechanism for the transformation **4**→**5**, we have proven that at low temperature only the carbon–chlorine bond is cleaved. Thus, performing the first step of the reaction with 3-pentanone or cyclopentanone as electrophiles, compounds **6a** and **6b** were isolated in 97 and 65% yield, respectively. These experiments demonstrated the participation of intermediates **VIII** for the first step and probably **IX** for the second one (Fig. 4).

Table 2. Preparation of compounds **3**

Entry	Diol **2**	Oxidation method[a]	Product[b]				
			No.	R^1	R^2	Yield (%)[c]	*trans*/α-*cis*/β-*cis*[d]
1	**2a**	A	**3a**	Pr^i	H	41	71:–:29
2	**2b**	A	**3b**	Bu^t	H	57	53:21:26
3	**2c**	B	**3c**	Me	Me	51	–
4	**2d**	B	**3d**	Et	Et	75	–
5	**2e**	B	**3e**	Cy	Cy	60	–
6	**2f**	B	**3f**	$(CH_2)_5$		58	–
7	**2g**	B	**3g**	$(CH_2)_2O(CH_2)_2$		56	–
8	**2j**	B	**3j**	Bu^t	Me	68	47:47:6
9	**2k**	B	**3k**	Ph	Me	53	36[e]:47:17[e]

[a] Corresponding to the last step (reaction (iii) in Scheme 3); Method A: $(Ph_3P)_3RuCl_2$; Method B: PCC.

[b] All products **3** were >95% pure (GLC and 300 MHz ^1H NMR) and were fully characterised by spectroscopic means (IR, ^1H and ^{13}C NMR, and mass spectrometry).

[c] Isolated yield after column chromatography (silica gel, hexane/diethyl ether) based on the corresponding starting diol **2**.

[d] Diastereomeric ratio determined by GLC; the corresponding assignments were made on the basis of NMR experiments on the isolated diastereoisomers (see text).

[e] These diastereoisomers could not be separated by column chromatography; assignments were carried out on the corresponding mixture.

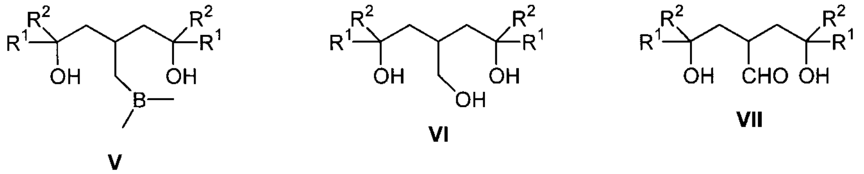
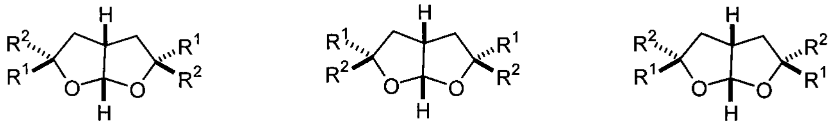
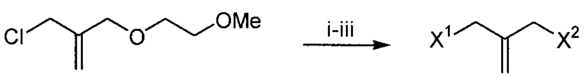


Figure 2.



trans α-*cis* β-*cis*

Figure 3.



4 **5**

Scheme 4. Reagents and conditions: (i) Li, $C_{10}H_8$ cat. (2.5%), E^1=Bu^{t}CHO, Et$_2$CO, (CH$_2$)$_5$CO, O(CH$_2$CH$_2$)$_2$CO, PhCOMe, Me$_3$SiCl, THF, −78 to −30 (or 0) °C; (ii) E^2=Bu^{t}CHO, Me$_2$CO, Et$_2$CO, Bu$^t_2$CO, (CH$_2$)$_4$CO, (CH$_2$)$_5$CO, Bu^{t}COMe, PhCH=NPh, Me$_3$SiCl, MeI, Bu^{n}Hal (Hal=Cl, Br, I), D$_2$O, THF, −30 (or 0) to 20°C; (iii) H$_2$O.

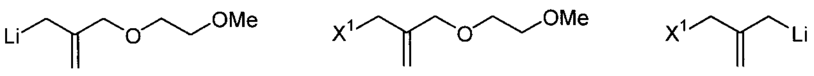
As a conclusion, we have reported herein the use of a new trimethylenemethane dianion synthon of type **III** for the introduction of two equal or different electrophiles in the isobutylene skeleton. For carbonyl compound derivatives, simple transformation (hydroboration–oxidation) of the unsaturated diols led to the expected perhydrofurofurans, which are structural units of important biologically active natural compounds.

Table 3. Preparation of compounds **5**

Entry	Electrophile E^1	Electrophile E^2	Product[a]			
			No.	X^1	X^2	Yield (%)[b]
1	Bu^{t}CHO	Et$_2$CO	**5a**	Bu^{t}CHOH	Et$_2$COH	43
2	Et$_2$CO	Bu^{t}CHO	**5a**	Et$_2$COH	Bu^{t}CHOH	34
3	Et$_2$CO	Me$_2$CO	**5b**	Et$_2$COH	Me$_2$COH	47
4	Et$_2$CO	Bu^{t}COMe	**5c**	Et$_2$COH	Bu^{t}C(OH)Me	44
5	Et$_2$CO	Bu$^t_2$CO	**5d**	Et$_2$COH	Bu$^t_2$COH	61
6	Et$_2$CO	PhCH=NPh	**5e**	Et$_2$COH	PhCHNHPh	34
7	Et$_2$CO	Me$_3$SiCl	**5f**	Et$_2$COH	Me$_3$Si	12
8	Et$_2$CO	D$_2$O	**5g**	Et$_2$COH	D	77
9	Et$_2$CO	MeI	**5h**	Et$_2$COH	Me	42
10	Et$_2$CO	Bu^{n}Cl	**5i**	Et$_2$COH	Bu^n	40
11	Et$_2$CO	Bu^{n}Br	**5i**	Et$_2$COH	Bu^n	45
12	Et$_2$CO	Bu^{n}I	**5i**	Et$_2$COH	Bu^n	38
13	(CH$_2$)$_5$CO	(CH$_2$)$_4$CO	**5j**	(CH$_2$)$_5$COH	(CH$_2$)$_4$COH	57
14	(CH$_2$)$_5$CO	PhCH=NPh	**5k**	(CH$_2$)$_5$COH	PhCHNHPh	25
15	O(CH$_2$CH$_2$)$_2$CO	(CH$_2$)$_5$CO	**5l**	O(CH$_2$CH$_2$)$_2$COH	(CH$_2$)$_5$COH	47
16	PhCOMe	(CH$_2$)$_5$CO	**5m**	PhC(OH)Me	(CH$_2$)$_5$COH	38
17	Me$_3$SiCl	Et$_2$CO	**5f**	Me$_3$Si	Et$_2$COH	75

[a] All products **5** were >95% pure (GLC and 300 MHz ^{1}H NMR) and were fully characterised by spectroscopic means (IR, ^{1}H and ^{13}C NMR, and mass spectrometry).

[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting chloroether **4**.



VIII

6a: X^1 = Et$_2$COH

6b: X^1 = (CH$_2$)$_4$COH

IX

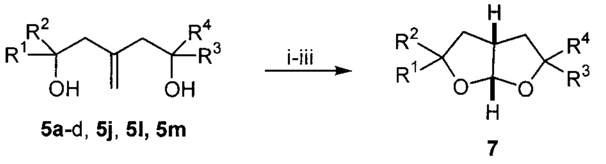
Figure 4.

Finally, we carried out the transformation of some of the compounds **5** into the corresponding differently substituted perhydrofurofurans **7** using the same methodologies used for compounds **3** (Scheme 5 and Table 4). Also here, when possible, the expected mixture of diastereoisomers (ca. 1:1) was obtained (Table 4, entries 1, 3, and 7, and footnote d).

Experimental

General

Melting points were obtained with a Reichert Thermovar apparatus. NMR spectra were recorded on a Bruker AC-300 (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR)



Scheme 5. Reagents and conditions: (i) BH_3·THF, 0°C; (ii) 33% H_2O_2, 3 M NaOH, 0°C; (iii) $(Ph_3P)_3RuCl_2$, PhH, 0°C (for R^2=H) or PCC, CH_2Cl_2, 0°C.

Table 4. Preparation of compounds **7**

Entry	Diol **5**	Oxidation method[a]	Product[b]					
			No.	R^1	R^2	R^3	R^4	Yield (%)[c]
1	**5a**	A	**7a**	Bu^t	H	Et	Et	36[d]
2	**5b**	B	**7b**	Et	Et	Me	Me	58
3	**5c**	B	**7c**	Et	Et	Bu^t	Me	53[d]
4	**5d**	B	**7d**	Et	Et	Bu^t	Bu^t	72
5	**5j**	B	**7j**	$(CH_2)_5$		$(CH_2)_4$		56
6	**5l**	B	**7l**	$(CH_2)_2O(CH_2)_2$		$(CH_2)_5$		47
7	**5m**	B	**7m**	Ph	Me	$(CH_2)_5$		47[d]

[a] Corresponding to the last step (reaction (iii) in Scheme 5); Method A: $(Ph_3P)_3RuCl_2$; Method B: PCC.

[b] All products **7** were >95% pure (GLC and 300 MHz ^{1}H NMR) and were fully characterised by spectroscopic means (IR, ^{1}H and ^{13}C NMR, and mass spectrometry).

[c] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the corresponding starting diol **5**.

[d] Obtained as a ca. 1:1 diastereomeric mixture (300 MHz ^{1}H 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 analyzer. The purity of volatile and the chromatographic analyses (GLC) were determined with a Hewlett Packard HP-5890 instrument equipped with a flame ionisation detector and a 12 m capillary column (0.2 mm diametre, 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 μm. Thin layer chromatography was carried out on TLC plastic sheets with silica gel 60 F_{254} (Merck). All starting compounds were of the best available grade (Acros, Aldrich, Fluka) and were used without further purification. THF was dried over benzophenone ketyl under an argon atmosphere and distilled before use.

Preparation of diols 2. General procedure

A solution of 3-chloro-2-chloromethylprop-1-ene (0.16 ml, 2 mmol) and the corresponding electrophile (3.96 mmol) in THF (6 ml) was added 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 room temperature continuing the stirring for 8 h. Then it was hydrolysed with water (10 ml), extracted with ethyl acetate (3×15 ml), and the organic phase was dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure (15 Torr), the resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield compounds **2**. Compounds **2a**, **2c**, **2d**, and **2f** were fully characterised by comparison of their chromatographic and spectral data with those reported in the literature.[23] For new compounds, physical and spectroscopic data follow:

***dl* and *meso*-2,2,8,8-Tetramethyl-5-methylidenenonane-3,7-diol (2b).** Colourless crystals; t_r 11.760 and 11.757; R_f 0.73 (hexane/ethyl acetate 1:1); mp 50–52°C; ν((KBr) 3394 (OH), 3072, 1645 (C=CH), and 1032 cm^{-1} (CO); δ_H 0.93 (36H, s, 12×CH_3), 2.00 (4H, dd, J=14.0, 11.0 Hz, 4×*H*CHCOH), 2.35 (4H, d, J=14.0 Hz, 4×HC*H*COH), 3.32 (4H, dd, J=11.0, 1.8 Hz, 4×CH), and 5.01 (4H, s, 4×H_2C=C); δ_C 25.7 (12×CH_3), 34.55 (4×*C*CH_3), 37.8(4×*C*H_2CO), 76.3 (4×CHOH), 115.55 (2×H_2*C*=C), and 145.3 (2×*C*=CH_2); m/z 174 (M^+−54, 1%), 57 (78), 55 (16), and 43 (100); HRMS calcd for $C_{14}H_{28}O_2$ 228.2089, (M^+−CH_5O) 195.1749, found 195.1743.

1,1,5,5-Tetracyclohexyl-3-methylidenepentane-1,5-diol (2e). Colourless crystals; mp 126–128°C; t_r 16.34; ν (KBr) 3250 (OH), 3062, 1633 (C=CH), and 1120 cm^{-1} (CO); δ_H (C_6D_6) 1.11–1.68, 1.78–1.91 [44H, 2m, 4×$(CH_2)_5$, 4×CH], 2.65 (4H, br s, 2×CH_2CO), and 4.94 (2H, s, H_2C=C); δ_C (C_6D_6) 27.15, 27.65, 27.8, 28.05 [4×$(CH_2)_5$], 42.05 (2×*C*H_2CO), 46.7 (2×CH), 77.75 (2×CO), 117.25 (H_2*C*=C), and 149.3 (*C*=CH_2); m/z 444 (M^+, <1%), 83 (100), and 55 (53); HRMS calcd for $C_{30}H_{52}O_2$ 444.3967, found 444.3984.

4-[2-(4-Hydroxytetrahydro-2H-pyran-4-ylmethyl)allyl]-tetrahydro-2H-pyran-4-ol (2g). Colourless oil; t_r 16.45; R_f 0.53 (methanol); ν (film) 3342 (OH), 3096, 1635 (C=CH), 1109, 1061, and 1026 cm^{-1} (CO); δ_H 1.66, 1.85 (8H, 2br s, 4×C*H*$_2$$CH_2$O), 1.91, 1.95, 2.31, 2.83 (4H, 4d, J=6.1, 13.4 Hz, 2×CH_2C=C), 3.39–3.93 (8H, m, 4×CH_2O) 4.78, 4.98 (2H, 2s, H_2C=C); δ_C 37.2, 37.85, 39.4 (2×*C*$H_2$$CH_2$O), 49.2, 51.35 (2×*C*$H_2$=C), 72.35, 73.9 (2×CO), 116.05 (H_2*C*=C), and 141.95 (*C*=CH_2); m/z 238 (M^+−18, <1%), 101 (77), 93 (20), 91 (13), 83 (100), 71 (58), and 55 (31); HRMS calcd for $C_{14}H_{24}O_4$ 256.1675, (M^+−H_2O) 238.1568, found 238.1553.

4-[2-(4-Hydroxytetrahydro-2H-4-thiopyranylmethyl)-allyl]tetrahydro-2H-thiopyran-4-ol (2h). Colourless oil; t_r 17.86; R_f 0.80 (methanol); ν (film) 3391 (OH), 3095, 1638

($C{=}CH$), and 1073 cm^{-1} (CO); δ_{H} 1.68–1.87 (8H, m, $4\times C\mathit{H}_2CH_2S$), 1.97 (2H, br s, 2×OH), 2.35 (4H, s, $2\times CH_2C{=}C$), 2.35–2.47, 2.63–2.94 (8H, 2m, $4\times CH_2S$), and 4.97 (2H, s, $H_2C{=}C$); δ_{C} 24.45 ($4\times \mathit{C}H_2CH_2S$), 39.0 ($2\times \mathit{C}H_2C{=}C$), 49.6 ($4\times CH_2S$), 70.1 (2×CO), 119.35 ($\mathit{C}H_2{=}C$), and 141.3 ($\mathit{C}{=}CH_2$); *m/z* 290 ($M^+ + 2$, <1%), 288 ($M^+$, <1%), 117 (70), 99 (100), 67 (10), and 55 (81); HRMS calcd for $C_{14}H_{24}O_2S_2$ 288.1217, found 288.1228.

4-[2-(4-Hydroxy-1-propyl-4-piperidylmethyl)allyl]-1-propylpiperidin-4-ol (2i). Colourless oil; t_r 20.21; R_f 0.18 (methanol); ν (film) 3369 (OH), 3066, 1629 ($C{=}CH$), 1139, 1065, and 1105 (CO, CN) cm^{-1}; δ_{H} 0.86 (6H, t, J=7.4 Hz, $2\times CH_3$), 1.41–1.80 (12H, m, $2\times C\mathit{H}_2CH_3$, $4\times CH_2C\mathit{H}_2CO$), 2.24–2.32 (8H, m, $4\times C\mathit{H}_2CH_2CO$), 2.36 (4H, s, $2\times CH_2C{=}C$), 2.53–2.65 (4H, m, $2\times C\mathit{H}_2CH_2CH_3$), and 4.91 (2H, s, $H_2C{=}C$); δ_{C} 12.05 ($2\times CH_3$), 20.25 ($2\times \mathit{C}H_2CH_3$), 37.65 ($4\times CH_2\mathit{C}H_2CO$), 49.6, 60.8 (6×CN), 49.7 ($2\times \mathit{C}H_2C{=}C$), 70.35 (2×CO), 118.45 ($H_2\mathit{C}{=}C$), and 142.35 ($\mathit{C}{=}CH_2$); *m/z* 320 ($M^+ - 18$, <1%), 114 (100), and 43 (93). HRMS calcd for $C_{20}H_{38}N_2O_2$ 338.2933, ($M^+ - H_2O$) 320.2828, found 320.2835.

dl and *meso*-2,2,3,7,8,8-Hexamethyl-5-methylidene-nonane-3,7-diol (2j) (*first diastereomer*). Colourless crystals; mp 50–52°C; t_r 13.82; R_f 0.62 (hexane/ethyl acetate 2:1); ν (film) 3404 (OH), 3060, 1637 ($C{=}CH$), and 1049 cm^{-1} (CO); δ_{H} 0.94 [18H, s, $2\times (CH_3)_3C$], 1.08 (6H, s, $2\times CH_3CO$), 2.08–2.32 (4H, m, $2\times CH_2CO$), and 4.83 (2H, s, $H_2C{=}C$); δ_{C} 21.2 ($2\times \mathit{C}H_3CO$), 25.30 [$2\times (\mathit{C}H_3)_3C$], 38.45 [$2\times \mathit{C}(CH_3)_3$], 42.05 ($2\times CH_2CO$), 76.0 (2×CO), 117.95 ($H_2\mathit{C}{=}C$), and 147.7 ($\mathit{C}{=}CH_2$); *m/z* 181 ($M^+ - 75$, 1%), 123 (11), 57 (44), and 44 (100); HRMS calcd for $C_{16}H_{32}O_2$ 256.2402, ($M^+ - H_3O_2$) 221.2269, found 221.2298. (*second diastereomer*): colourless crystals; mp 50–52°C; t_r 13.91; R_f 0.62 (hexane/ethyl acetate 2:1); ν (film) 3404 (OH), 3060, 1637 ($C{=}CH$), and 1049 cm^{-1} (CO); δ_{H} 0.96 [18H, s, $2\times (CH_3)_3C$], 1.15 (6H, s, $2\times CH_3CO$), 2.37–2.49 (4H, m, $2\times CH_2CO$), and 4.98 (2H, s, $H_2C{=}C$); δ_{C} 22.5 ($2\times \mathit{C}H_3CO$), 25.40 [$2\times (\mathit{C}H_3)_3C$], 38.15 [$\mathit{C}(CH_3)_3$], 43.55 ($2\times CH_2CO$), 76.6 (2×CO), 118.4 ($H_2\mathit{C}{=}C$), and 146.1 ($\mathit{C}{=}CH_2$); *m/z* 163 ($M^+ - 93$, 1%), 123 (11), 101 (14), 83 (13), 57 (48), 44 (100), and 43 (58). HRMS calcd for $C_{16}H_{32}O_2$ 256.2402, ($M^+ - H_3O_2$) 221.2269, found 221.2298.

4-Methylidene-2,6-diphenylheptane-2,6-diol (2k). Colourless oil; t_r 15.81; R_f 0.75 (hexane/ethyl acetate 1:1); ν (film) 3402 (OH), 3060, 3023, 1637 ($C{=}CH$), and 1051 cm^{-1} (CO); δ_{H} 1.46, 1.50 (6H, 2s, $2\times CH_3$), 2.28–2.57 (2H, m, CH_2CO), 4.76, 4.85 (2H, 2s, $H_2C{=}C$), and 7.18–7.38 (10H, m, ArH); δ_{C} 29.9, 30.55 ($2\times CH_3$), 50.35, 50.45 ($2\times CH_2CO$), 74.0, 74.3 (2×CO), 119.55, 119.65 ($2\times H_2\mathit{C}{=}C$), 124.75, 124.8, 126.45, 126.55, 128.0, 142.75, 143.05, 147.9, and 148.1 (12×ArC and $\mathit{C}{=}CH_2$); *m/z* 260 ($M^+ - 36$, 1%), 143 (69), 105 (54), 91 (15), 77 (51), and 43 (100); HRMS calcd for $C_{20}H_{24}O_2$ 296.1776, ($M^+ - 2H_2O$) 260.1565, found 260.1564.

dl and *meso*-3,7-Dimethyl-5-methylidenenonane-3,7-diol (2l). Colourless oil; t_r 11.29; R_f 0.23 (hexane/diethyl ether 2:1); ν (film) 3425 (OH), 3068, 1633 ($C{=}CH$), and 1059 cm^{-1} (CO); δ_{H} 0.90, 0.91 (12H, 2t, J=7.6 Hz, $4\times C\mathit{H}_3CH_2$), 1.13, 1.14 (12H, 2s, $4\times CH_3CO$), 1.49 (8H, q, J=7.6 Hz, $4\times C\mathit{H}_2CH_3$), 2.04–2.54 (4H, 2m, $4\times CH_2C{=}C$), and 4.91 (4H, d, J=2.1 Hz, $2\times H_2C{=}C$); δ_{C} 8.35 ($4\times \mathit{C}H_3CH_2$), 26.35, 26.6 ($4\times \mathit{C}H_3CO$), 35.15, 35.6 ($4\times \mathit{C}H_2CH_3$), 47.5, 47.6 ($4\times \mathit{C}H_2C{=}C$), 73.0 (4×CO), 117.75, 117.8 ($2\times H_2\mathit{C}{=}C$), and 144.25 ($2\times \mathit{C}{=}CH_2$); *m/z* 153 ($M^+ - 47$, <1%), 73 (36), and 43 (100); HRMS calcd for $C_{12}H_{24}O_2$ 200.1766, ($M^+ - CH_5O$) 167.1436, found 167.1452.

3-Trimethylsilyl-2-(trimethylsilylmethyl)prop-1-ene (2m). Colourless oil; t_r 7.26; R_f 0.91 (hexane/ethyl acetate 5:1); ν (film) 3073, 1629 ($C{=}CH$), and 1252 (CSi) cm^{-1}; δ_{H} 0.05 (18H, s, $6\times CH_3$), 1.49 (4H, s, $2\times CH_2Si$), and 4.39 (2H, s, $H_2C{=}C$); δ_{C} −1.3 ($6\times CH_3$), 29.3 ($2\times CH_2Si$), 105.5 ($H_2\mathit{C}{=}C$), and 145.1 ($\mathit{C}{=}CH_2$); *m/z* 202 ($M^+ + 2$, <1%), 200 (M^+, 8%), 185 (11), 112 (45), 97 (21), and 73 (100); HRMS calcd for $C_{10}H_{24}Si_2$ 200.1417, found 200.1420.

3-Methylsulfanyl-2-methylsulfanylmethylprop-1-ene (2n). Colourless oil; t_r 9.15; R_f 0.56 (hexane/ethyl acetate 5:1); ν (film) 3078, 1653 ($C{=}CH$) cm^{-1}; δ_{H} 1.95 (6H, s, $2\times CH_3$), 3.24 (4H, s, $2\times CH_2S$), and 4.96 (2H,s, $H_2C{=}C$); δ_{C} 14.75 ($2\times CH_3$), 37.5 ($2\times CH_2S$), 115.25 ($H_2\mathit{C}{=}C$), and 139.9 ($\mathit{C}{=}CH_2$); *m/z* 150 ($M^+ + 2$, <1%), 148 (M^+, 8%), 101 (54), 85 (100), and 47 (14); HRMS calcd for $C_6H_{12}S_2$ 148.0380, found 148.0386.

Hydroboration–oxidation of diols 2. General procedure

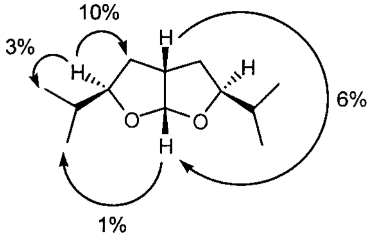
1 M $BH_3\cdot THF$ (5 mmol) was added to the corresponding alkene (1 mmol) and the mixture was stirred for 6 h at room temperature. Then, water (5 ml) was added at 0°C and after 5 min, 3 M NaOH (10 ml) and H_2O_2 (33% vol.) (10 ml) were added successively, maintaining the stirring for 8 h. The reaction mixture was extracted with ethyl acetate (3×15 ml), and the organic phase was dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure (15 Torr), the corresponding triols were obtained and used in the next step without further purification.

Preparation of the perhydrofuro[2,3-*b*]furans 3a and 3b. General procedure

The complex $RuCl_2(Ph_3P)_3$ (767 mg, 0.8 mmol) was added to a solution of the corresponding triol (1 mmol) derived from **2** 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/ethyl acetate) to yield the expected products **3a** and **3b**. Their physical and spectroscopic data follow:

(2*R,3a*S**,5*R**,6a*R**)-2,5-Diisopropylperhydrofuro[2,3-*b*]furan (*trans*-3a).** Colourless oil; t_r 10.82; R_f 0.12 (hexane/ethyl acetate 5:1); ν (film) 1031 cm^{-1} (CO); δ_{H} 0.86, 0.88 (6H, 2d, J=6.4, 6.7 Hz, $2\times CH_3$), 0.99 (6H, d, J=6.7 Hz, $2\times CH_3$), 1.18–1.28 (2H, m, $2\times C\mathit{H}CH_3$), 1.51–1.86 (4H, m, $2\times CH_2$), 2.72–2.89 (1H, m, $CH_2C\mathit{H}CH_2$), 3.41–3.49, 3.65–3.89 (2H, 2m, $2\times CH_2C\mathit{H}O$), and 5.30 (1H, d, J=5.5 Hz, OCHO); δ_{C} 18.35, 18.4, 19.65, 19.75 ($4\times CH_3$), 32.55, 32.95 (2×$CHCH_3$), 35.0, 35.95 (2×CH_2), 43.2 (CH_2CHCH_2), 82.75, 84.4 (2×$COCH_2$), and 108.5 (OCO); *m*/*z* 156 (M^+-42, 5%), 155 (48), 137 (13), 109 (14), 69 (52), 55 (36), 44 (100), and 43 (71); HRMS calcd for $C_{12}H_{22}O_2$ 198.1620, found 198.1592.

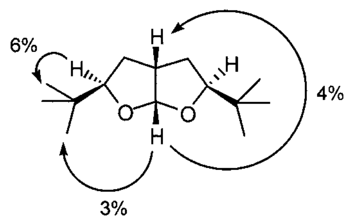
(2*R*, 3a*S*, 5*S*, 6a*R*)-2,5-Diisopropylperhydrofuro[2,3-*b*]furan (β-*cis*-3a). Colourless oil; t_r 10.97; R_f 0.12 (hexane/ethyl acetate 5:1); ν (film) 1031 cm^{-1} (CO); δ_H 0.84, 0.99 (12×H, 2d, J=6.4 Hz, 4×CH_3), 1.18–1.23 (2H, m, 2×C*H*CH_3), 1.54–1.67, 1.71–1.80 (4H, 2m, 2×CH_2), 2.85–2.98 (1H, m, CH_2C*H*CH_2), 3.74–3.90 (2H, 2m, 2×CH_2C*H*O), and 5.70 (1H, d, J=5.2 Hz, OCHO); δ_C 18.3, 18.4, 19.45, 19.5 (4×CH_3), 32.55, 32.95 (2×*C*HCH_3), 35.0, 36.0 (2×CH_2), 43.15 (CH_2*C*HCH_2), 85.35, 86.65 (2×*C*OCH_2), and 108.75 (OCO); *m*/*z* 156 (M^+-42, 7%), 155 (64), 137 (14), 109 (17), 69 (62), 55 (43), 44 (100), and 43 (82); HRMS calcd for $C_{12}H_{22}O_2$ 198.1620, found 198.1592.



(2*R, 3a*S**, 5*R**, 6a*R**)-2,5-Di(*tert*-butyl)perhydrofuro-[2,3-*b*]furan (*trans*-3b).** Colourless oil; t_r 11.75; R_f 0.77 (hexane/diethyl ether 3:2); ν (film) 1128 cm^{-1} (CO); δ_H 0.89, 0.92 [18H, 2s, 2×$(CH_3)_3C$], 1.33–1.45, 1.63–1.76 (4H, 2m, 2×CH_2), 2.73–2.82 (1H, m, CH_2C*H*CH_2), 3.50–3.55, 3.74–3.80 (2H, 2m, 2×CH_2C*H*O), and 5.57 (1H, d, J=5.5 Hz, OCHO); δ_C 25.6, 25.95 (6×CH_3), 32.15, 33.0 (2×CH_2), 43.1 (CH_2*C*HCH_2), 85.2, 86.9 (2×*C*OCH_2), and 108.5 (OCO); *m*/*z* 193 (M^+-33, <1%), 169 (100), 109 (26), 107 (73), 57 (71), 55 (61), and 43 (83). HRMS calcd for $C_{14}H_{26}O_2$ 226.1933, (M^++1) 227.2011, found 227.1990.

(2*R*, 3a*R*, 5S, 6a*S*)-2,5-Di(*tert*-butyl)perhydrofuro[2,3-*b*]furan (α-*cis*-3b). Colourless oil; t_r 12.00; R_f 0.77 (hexane/diethyl ether 3:2); ν (film) 1050 cm^{-1} (CO); δ_H 0.92 [18H, s, 2×$(CH_3)_3C$], 1.22–1.47 (4H, m, 2×CH_2), 2.65–2.71 (1H, m, CH_2C*H*CH_2), 3.50–3.56 (2H, m, 2×CH_2C*H*O), and 5.40 (1H, d, J=5.2 Hz, OCHO); δ_C 25.55 (6×CH_3), 33.15 (2×CH_2), 42.75 (CH_2*C*HCH_2), 89.0 (2×*C*OCH_2), and 108.3 (OCHO); *m*/*z* 211 (M^+-15, <1%), 169 (69), 151 (15), 123 (14), 109 (23), 107 (62), 57 (61), 55 (53), 44 (100), and 43 (82); HRMS calcd for $C_{14}H_{26}O_2$ 226.1933, ($M^+-C_2H_5$) 197.1541, found 197.1554.

(2*R*, 3a*S*, 5*S*, 6a*R*)-2,5-Di(*tert*-butyl)perhydrofuro[2,3-*b*]furan (β-*cis*-3b). Colourless oil; t_r 11.85; R_f 0.77 (hexane/diethyl ether 3:2); ν (film) 1074 cm^{-1} (CO); δ_H 0.87 [18H, s, 2×$(CH_3)_3C$], 1.57–1.62, 1.79–1.86 (4H, 2m, 2×CH_2), 2.69–2.87 (1H, m, CH_2C*H*CH_2), 3.83–3.96 (2H, m, 2×CH_2C*H*O), and 5.67 (1H, d, J=5.0 Hz, OCHO); δ_C 25.7 (6×CH_3), 33.45, 33.6 (2×CH_2), 42.95 (CH_2*C*HCH_2), 87.45 (2×*C*OCH_2), and 109.15 (OCO); *m*/*z* 193 (M^+-33, <1%), 169 (100), 151 (13), 123 (17), 109 (27), 107 (73), 57 (76), 55 (67), 44 (73), and 43 (89). HRMS calcd for $C_{14}H_{26}O_2$ 226.1933, (M^++1) 227.2011, found 227.2020.



Preparation of the perhydrofuro[2,3-*b*]furans 3c–g, 3j, and 3k. General procedure

Pyridinium chlorochromate (2.4 mmol, 254 mg) was added to a solution of the corresponding triol (1 mmol) derived from **2** 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/ethyl acetate) to yield the expected products. Their physical and spectroscopic data follow:

2,2,5,5-Tetramethylperhydrofuro[2,3-*b*]furan (3c). Colourless oil; t_r 6.44; R_f 0.27 (hexane/ethyl acetate 7:3); ν (film) 1090 and 1024 cm^{-1} (CO); δ_H 1.20, 1.41 (12H, 2s, 4×CH_3), 1.69, 2.00 (4H, 2dd, J=12.8, 5.5 and 12.8, 9.8 Hz, 2×CH_2), 3.0 (1H, ddd, J=12.8, 9.8, 5.5 Hz, C*H*CH_2), and 5.66 (1H, d, J=5.5 Hz, OCHO); δ_C 29.2, 29.3 (4×CH_3), 44.5 (*C*HCH_2), 44.95 (2×CH_2), 83.25 (2×*C*OCH_2), and 109.35 (OCO); *m*/*z* 170 (M^+, <1%), 155 (36), 109 (20), 55 (20), and 43 (100); HRMS calcd for $C_{10}H_{18}O_2$ 170.1307, (M^+-CH_3) 155.1072, found 155.1049.

2,2,5,5-Tetraethylperhydrofuro[2,3-*b*]furan (3d). Colourless oil; t_r 12.51; R_f 0.10 (hexane/ethyl acetate 5:1); ν (film) 1034 cm^{-1} (CO); δ_H 0.83–0.91 (12H, m, 4×CH_3), 1.18–1.23, 1.34–1.81, 1.89–1.97 (12H, 3m, 6×CH_2), 2.83–2.92 (1H, m, C*H*CH_2), and 5.61 (1H, d, J=5.5 Hz, OCHO); δ_C 8.2, 8.85 (4×CH_3), 30.85, 31.6 (4×*C*H_2CH_3), 41.0 (2×*C*H_2CH), 43.7 (*C*HCH_2), 88.7 (2×*C*OCH_2), and 108.95 (OCO); *m*/*z* 199 (M^+-27, <1%), 197 (40), 107 (79), 57 (100), and 55 (55); HRMS calcd for $C_{14}H_{26}O_2$ 226.1933, ($M^+-C_2H_5$) 197.1542, found 197.1549.

2,2,5,5-Tetracyclohexylperhydrofuro[2,3-*b*]furan (3e). Colourless crystals; mp 158–160°C; R_f 0.81 (hexane/ethyl acetate 5:1); ν (KBr) 1110 cm^{-1} (CO); δ_H 0.83–2.89 (48H, m, 22×CH_2, 4×cyclohexyl CH), 2.66–2.89 (1H, m, C*H*CHO), and 5.61 (1H, d, J=6.1 Hz, OCHO); δ_C 22.7, 26.65, 26.8, 27.0, 27.1, 27.6, 28.25, 28.55, 28.95, 29.35, 29.7, 31.95, 37.55 (22×CH_2), 44.55, 45.05, 45.55 (4×cyclohexyl CH, *C*HCHO), 94.65 (2×*C*OCH_2), and 110.8 (OCO); Anal. calcd for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38; found C, 81.19; H, 11.58.

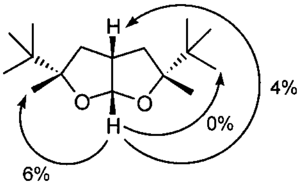
Dispiro[cyclohexane-1,2′-perhydrofuro[2,3-*b*]furan-5′,1″-cyclohexane] (3f). Colourless oil; t_r 15.78; R_f 0.68 (hexane/diethyl ether 2:1); ν (film) 1018 cm^{-1} (CO); δ_H 1.20–1.81 [20H, m, 2×$(CH_2)_5$], 1.98 (4H, dd, J=12.8, 9.5 Hz, 2×C*H*$_2$CH), 2.90 (1H, m, C*H*CH_2), and 5.64 (1H, d, J=5.2 Hz, OCHO); δ_C 23.35, 23.75, 25.50, 38.2 [2×$(CH_2)_5$)], 43.05 (*C*HCH_2), 85.3 (2×*C*OCH_2), and

108.15 (OCO); *m/z* 251 ($M^+ +1$, 3%), 250 (M^+, 21%), 232 (15), 83 (10), 55 (100), and 54 (14); HRMS calcd for $C_{16}H_{26}O_2$ 250.1932, found 250.2014.

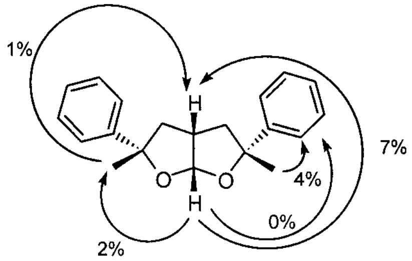
Dispiro[1-oxacyclohexane-4,2′-perhydrofuro[2,3-*b*]furan-5′,4″-1″-oxacyclohexane] (3g). Colourless oil; t_r 14.39; R_f 0.13 (hexane/ethyl acetate 4:1); ν (film) 1101 and 1019 cm^{-1} (CO); δ_H 1.52–1.85 (12H, m, $4\times CH_2CH_2CO$, $2\times CH_2CH$), 2.87–3.04 (1H, m, $CHCH_2$), 3.61–3.69, 3.77–3.89 (8H, 2m, $4\times CH_2O$), and 5.70 (1H, d, $J=5.5$ Hz, OCHO); δ_C 38.15, 38.8, 43.85 ($4\times CH_2CH_2O$, $2\times CH_2CH$), 42.55 ($CHCH_2$), 64.85, 65.15 ($4\times CH_2O$), 82.15 ($2\times COCH_2CH$), and 108.55 (OCO); *m/z* 254 (M^+, 21%), 109 (25), 96 (88), 83 (65), 55 (78), 54 (12), and 41 (100); HRMS calcd for $C_{14}H_{22}O_4$ 254.1518, found 254.1544.

(2*R, 3a*S**, 5*R**, 6a*R**)-2,5-Di(*tert*-butyl)-2,5-dimethylperhydrofuro[2,3-*b*]furan (*trans*-3j).** Colourless oil; t_r 13.25; R_f 0.33 (hexane/diethyl ether 3:2); ν (film) 1100 cm^{-1} (CO); δ_H 0.88, 0.99 [18H, 2s, $2\times(CH_3)_3C$], 1.13, 1.37 (6H, 2s, $2\times CH_3CO$), 1.72–1.88 (4H, m, $2\times CH_2$), 2.81–3.05 (1H, m, $CHCH_2$), and 5.64 (1H, d, $J=5.5$ Hz, OCHO); δ_C 21.85, 25.2 ($2\times CH_3CO$), 25.35, 25.75 [$2\times(CH_3)_3C$], 36.45 [$2\times C(CH_3)_3$], 39.25, 39.75 ($2\times CH_2$), 49.05 ($CHCH_2$), 89.9, 91.9 ($2\times COCH_2$), and 109.95 (OCO); *m/z* 253 ($M^+ -1$, <1%), 197 (32), 57 (81), 55 (27), and 43 (100). HRMS calcd for $C_{16}H_{30}O_2$ 254.2245, ($M^+ -C_4H_9$) 197.1542, found 197.1546.

(2*R*, 3a*R*, 5*S*, 6a*S*)-2,5-Di(*tert*-butyl)-2,5-dimethylperhydrofuro[2,3-*b*]furan (α-*cis*-3j). Colourless oil; t_r 13.15; R_f 0.33 (hexane/diethyl ether 3:2); ν (film) 1082 and 1028 cm^{-1} (CO); δ_H 0.97 [18H, s, $2\times(CH_3)_3C$], 1.14 (6H, s, $2\times CH_3CO$), 1.66–1.84 (4H, m, $2\times CH_2$), 2.93–3.07 (1H, m, $CHCH_2$), and 5.60 (1H, d, $J=6.1$ Hz, OCHO); δ_C 22.3 ($2\times CH_3CO$), 25.7 [$2\times(CH_3)_3C$], 36.3 [$2\times C(CH_3)_3$], 38.6 ($2\times CH_2$), 42.05 ($CHCH_2$), 91.3 ($2\times COCH_2$), and 107.9 (OCO); *m/z* 240 ($M^+ -14$, <1%), 197 (55), 57 (66), 55 (26), and 43 (100); HRMS calcd for $C_{16}H_{30}O_2$ 254.2245, found 254.2233.



(2*R*, 3a*R*, 5*S*, 6a*S*)-2,5-Dimethyl-2,5-diphenylperhydrofuro[2,3-*b*]furan (α-*cis*-3k). Colourless oil; t_r 16.81; R_f 0.65 (hexane/diethyl ether 3:2); ν (film) 1047 cm^{-1} (CO); δ_H 1.44 (6H, s, $2\times CH_3$), 1.88–1.94, 2.13–2.21 (4H, 2m, $2\times CH_2$), 3.13–3.22 (1H, m, $CHCH_2$), 6.05 (1H, d, $J=5.5$ Hz, OCHO), 7.04–7.11, and 7.20–7.54 (10H, 2m, ArH); δ_C 31.4 ($2\times CH_3$), 43.5 ($2\times CH_2$), 44.45 ($CHCH_2$), 86.85 ($2\times CCH_3$), 109.6 (OCHO), and 124.75, 127.6, 126.05, 147.6 ($12\times$ArC); *m/z* 281 ($M^+ -13$, <1%), 280 (10), 279 (49), 105 (100), 91 (29), 77 (34), and 44 (91). HRMS calcd for $C_{20}H_{22}O_2$ 294.1620, ($M^+ -CH_3$) 279.1385, found 279.1363.



(2*R, 3a*S**, 5*R**, 6a*R**) and (2*R*, 3a*S*, 5*S*, 6a*R*)-2,5-Dimethyl-2,5-diphenylperhydrofuro[2,3-*b*]furan (*trans*-3k and β-*cis*-3k).** Colourless oil; t_r 17.36, 17.89; R_f 0.65 (hexane/diethyl ether 3:2); ν (film) 1047 cm^{-1} (CO); δ_H 1.23, 1.52, 1.73 (12H, s, $4\times CH_3$), 2.11–2.25, 2.51–2.61 (8H, 2m, $4\times CH_2$), 2.66–2.81 (2H, m, $2\times CHCH_2$), 5.79, 5.95 (2H, 2d, $J=5.5$, 5.8 Hz, 2×OCHO), and 7.18–7.61 (20H, m, ArH); δ_C 29.85, 31.55, 32.7 ($4\times CH_3$), 43.6, 43.8, 43.95 ($4\times CH_2$), 44.1 ($2\times CHCH_2$), 87.1, 87.3 ($4\times CCH_3$), 109.15, 109.6 (2×OCO), 124.35, 124.4, 125.45, 126.4, 127.8, 128.1, 128.2, 128.05, and 148.1 ($24\times$ArC); *m/z* (t_r 17.36) 281 ($M^+ -13$, <2%), 105 (13), 91 (10), and 44 (100); *m/z* (t_r 17.89) 281 ($M^+ -13$, <1%), 105 (12), and 44 (100); HRMS calcd for $C_{20}H_{22}O_2$ 294.1620, ($M^+ +1$) 295.1698, found 295.1674.

Preparation of 2-chloromethyl-3-(2-methoxyethoxy)-prop-1-ene (4)

Dry THF (14 ml) was added to NaH (60% dispersion in mineral oil) (890 mg, 22 mmol), previously washed with dry toluene, the resulting suspension was cooled to 0°C and then a solution of 2-methoxyethan-1-ol (1.6 ml, 20 mmol) in THF (14 ml) was added. After stirring for 30 min, 3-chloro-2-(chloromethyl)prop-1-ene (2.43 ml, 21 mmol) was added and the stirring continued for 8 h. The mixture was hydrolysed with water (50 ml), extracted with ethyl acetate (3×40 ml), the organic phase was dried over anhydrous sodium sulfate, and the solvent removed by distillation under reduced pressure (15 Torr). The residue obtained was purified by column chromatography (silica gel, hexane/ethyl acetate) to furnish compound **4** in 40% yield. Its physical and spectroscopic data follow:

2-Chloromethyl-3-(2-methoxyethoxy)prop-1-ene (4). Colourless oil; t_r 7.40; R_f 0.83 (hexane/ethyl acetate 4:1); ν (film) 3067, 1656 (C=CH), 1199, and 1045 cm^{-1} (CO); δ_H 3.34 (3H, s, CH_3), 3.53 (4H, m, OCH_2CH_2O), 4.06 (4H, s, CH_2Cl and $C{=}CCH_2O$), 5.20, and 5.25 (2H, 2s, $H_2C{=}C$); δ_C 45.05 (CH_2Cl), 59.0 (CH_3), 69.5, 71.25, 71.8 ($3\times CH_2O$), 116.8 ($H_2C{=}C$), and 141.9 ($C{=}CH_2$); *m/z* 129 ($M^+ -35.5$, 35%), 59 (100), and 45 (99); HRMS calcd for $C_7H_{13}ClO_2$ 164.0604, found 164.0620.

Preparation of compounds 5. General procedure

A solution of chloroether **4** (329 mg, 2 mmol) and the corresponding first electrophile (1.98 mmol) in THF (6 ml) was added dropwise 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. After finishing the addition the mixture was warmed up to −30°C (0°C for compounds **5e–i** and **5k**) then a solution of the corresponding second electrophile (4 mmol) in THF (6 ml) was added dropwise for 1.5 h (only 0.5 min for compounds **5f** and **5g**). The stirring was maintained for 8 h allowing the mixture to reach room temperature. Then it was hydrolysed with water (10 ml), extracted with ethyl acetate (3×15 ml), and the organic phase was dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure (15 Torr) the resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield compounds **5**. 3-Ethyl-5-trimethylsilylmethylhex-5-en-3-ol (**5f**) has been previously reported.[31] For the rest of compounds **5** physical and spectroscopic data follow:

7-Ethyl-2,2-dimethyl-5-methylidenenonane-3,7-diol (5a). Colourless oil; t_r 12.42; R_f 0.22 (hexane/ ethyl acetate 7:3); ν (film) 3384 (OH), 3070, 1629 (C=CH), and 925 cm^{-1} (CO); δ_H 0.87 (6H, t, J=7.3 Hz, $2\times CH_3CH_2$), 0.92 (9H, s, $(CH_3)_3C$), 1.42–1.54 (4H, m, $2\times CH_2CH_3$), 2.19–2.32, 2.41–2.49 (4H, 2m, $2\times CH_2C{=}C$), 3.36 (1H, dd, J=10.4, 1.8 Hz, CH), 4.92, 5.01 (2H, 2s, $H_2C{=}C$); δ_C 7.9, 8.00 ($2\times CH_3CH_2$), 25.65 [$(CH_3)_3C$], 30.7, 31.1 ($2\times CH_2CH_3$), 34.7 [$C(CH_3)_3$], 39.75, 44.15 ($2\times CH_2C{=}C$), 65.8 (CH), 74.95 ($COCH_2CH_3$), 116.3 ($H_2C{=}C$), and 145.35 ($C{=}CH_2$); *m*/*z* 199 (M^+-29, <1%), 87 (100), 57 (92), 55 (25), and 45 (71); HRMS calcd for $C_{14}H_{28}O_2$ 228.2089, ($M^+-C_2H_5$) 199.1714, found 199.1698.

6-Ethyl-2-methyl-4-methylidenoctane-2,6-diol (5b). Colourless oil; t_r 10.86; R_f 0.125 (hexane/ethyl acetate 5:1); ν (film) 3371 (OH), 3072, 1637 (C=CH), and 1138 cm^{-1} (CO); δ_H 0.86 (6H, t, J=7.5 Hz, $2\times CH_3CH_2$), 1.22 (6H, s, $2\times CH_3CO$), 1.47 (4H, q, J=7.5 Hz, $2\times CH_2CH_3$), 2.20–2.60 (2H, br s, $2\times OH$), 2.38, 2.42 (4H, 2s, $2\times CH_2C{=}C$), and 5.26 (2H, s, $H_2C{=}C$); δ_C 8.0 ($2\times CH_3CH_2$), 30.1 ($2\times CH_3CO$), 31.25 ($2\times CH_2CH_3$), 44.95, 49.85 ($2\times CH_2C{=}C$), 70.95 ($COCH_3$), 75.05 ($COCH_2CH_3$), 117.85 ($H_2C{=}C$), and 144.25 ($C{=}CH_2$); *m*/*z* 164 (M^+-36, 3%), 135 (17), 107 (12), 57 (100), 55 (29), 44 (100), and 43 (88); HRMS calcd for $C_{12}H_{24}O_2$ 200.1776, (M^+-H_3O) 181.1592, found 181.1617.

7-Ethyl-2,2,3-trimethyl-5-methylidenenonane-3,7-diol (5c). Colourless crystals; mp 85–87°C; t_r 13.23; R_f 0.38 (hexane/ ethyl acetate 5:1); ν (KBr) 3320 (OH), 3068, 1628 (C=CH), and 1113 cm^{-1} (CO); δ_H 0.84, 0.88 (6H, 2t, J=7.2, 7.6 Hz, $2\times CH_3CH_2$), 0.95 [9H, s, $(CH_3)_3C$], 1.09 (3H, s, CH_3CO), 1.45, 1.46 (4H, 2q, J=7.2, 7.6 Hz, $2\times CH_2CH_3$), 2.18, 2.74 (4H, 2m, $2\times CH_2C{=}C$), 4.86, 4.90 (2H, 2s, $H_2C{=}C$); δ_C 7.65, 8.35 ($2\times CH_3CH_2$), 21.4 (CH_3CO), 25.35 [$(CH_3)_3C$], 30.55, 32.3 ($2\times CH_2CH_3$), 42.2, 44.8 ($2\times CH_2C{=}C$), 75.2, 76.5 ($2\times CO$), 117.9 ($H_2C{=}C$), and 145.2 ($C{=}CH_2$); *m*/*z* 177 (M^+-65, 2%), 149 (17), 57 (98), 55 (28), 45 (20), 44 (100), and 43 (88); HRMS calcd for $C_{15}H_{30}O_2$ 242.2245, found 242.2173.

3-(*tert*-Butyl)-7-ethyl-2,2-dimethyl-5-methylidenenonane-3,7-diol (5d). Colourless crystals; mp 63–65°C; t_r 14.91; R_f 0.49 (hexane/ethyl acetate 5:1); ν (KBr) 3425 (OH), 3068, 1628 (C=CH), and 1105 cm^{-1} (CO); δ_H 0.86 (6H, t, J=7.5 Hz, $2\times CH_3CH_2$), 1.10 [18H, s, $2\times(CH_3)_3C$], 1.46 (4H, 2m, $2\times CH_2CH_3$), 2.51, 2.66 (4H, 2s, $2\times CH_2C{=}C$), 4.82, and 4.96 (2H, 2s, $H_2C{=}C$); δ_C 8.05 ($2\times CH_3CH_2$), 29.45 [$2\times(CH_3)C$], 31.4 ($2\times CH_2CH_3$), 39.95 [$2\times C(CH_3)_3$], 42.45, 45.75 ($2\times CH_2C{=}C$), 75.1 ($COCH_2CH_3$), 82.2 [$CO(CH_3)_3$], 117.3 ($H_2C{=}C$), and 147.75 ($C{=}CH_2$); *m*/*z* 209 (M^+-75, 3%), 57 (100), and 43 (11); HRMS calcd for $C_{18}H_{36}O_2$ 284.2715, ($M^+-C_4H_{11}O$) 209.1905, found 209.1917.

5-(2-Anilino-2-phenylethyl)-3-ethylhex-5-en-3-ol (5e). Brown oil; t_r 19.46; R_f 0.20 (hexane/ethyl acetate 7:3); ν (film) 3564 (OH), 3406 (NH), 3060, 3026, 1601, 1495 (C=CH), and 917 cm^{-1} (CO); δ_H 0.85, 0.87 (6H, 2t, J=7.3 Hz, $2\times CH_3CH_2$), 1.47 (4H, q, J=7.3 Hz, $2\times CH_2CH_3$), 2.20, 2.13 (2H, AB system, J_{AB}=10.1 Hz, $C{=}CCH_2CO$), 2.47, 2.78 (2H, 2dd, J=14.3, 10.1 and 14.3, 3.8 Hz, CH_2CN), 4.45 (1H, dd, J=10.1, 3.8 Hz, CHN), 4.96, 5.06 (2H, 2s, $H_2C{=}C$), 6.46–6.60, 6.62–6.64, and 7.04–7.40 (10H, 3m, ArH); δ_C 8.0, 8.05 ($2\times CH_3$), 30.6, 31.5 ($2\times CH_2CH_3$), 43.4 (CH_2CN), 47.55 ($C{=}CCH_2CO$), 56.35 (CN), 75.05 (CO), 113.4 ($H_2C{=}C$), 117.15, 117.25, 126.15, 126.8, 128.55, 128.95, 143.95, 147.6 (12×ArC), and 144.45 ($C{=}CH_2$); *m*/*z* 267 (M^+-56, 22%), 266 (100), 77 (12), and 55 (11); HRMS calcd for $C_{22}H_{29}NO$ 323.2249, found 323.2239.

6-Deuterio-3-ethyl-5-methylidenehexan-3-ol (5g). Colourless oil; t_r 6.42; R_f 0.27 (hexane/ethyl acetate 5:1); ν (film) 3375 (OH), 3033, 1596 (C=CH), and 1031 cm^{-1} (CO); δ_H 0.79 (6H, t, J=7.3 Hz, $2\times CH_3CH_2$), 1.39 (4H, d, J=7.3 Hz, $2\times CH_2CH_3$), 1.74 (2H, br s, CH_2D), 2.08 (2H, s, $C{=}CCH_2CO$), 4.67, and 4.83 (2H, 2s, $H_2C{=}C$); δ_C 7.95 ($2\times CH_3$), 24.7 (t, J=19.5 Hz, CH_2D), 31.25 ($2\times CH_2CH_3$), 46.15, ($C{=}CCH_2CO$), 114.6 ($H_2C{=}C$), and 142.75 ($C{=}CH_2$); *m*/*z* 114 (M^+-30, 3%), 87 (71), 69 (20), and 57 (100); HRMS calcd for $C_9H_{17}DO$ 143.1436, (M^+-OH) 126.1406, found 126.1408.

3,5-Diethylhex-5-en-3-ol (5h). Colourless oil; t_r 7.81; R_f 0.14 (hexane/ethyl acetate 5:1); ν (film) 3425 (OH), 3080, 3024, 1634 (C=CH), and 1017 cm^{-1} (CO); δ_H 0.89 (6H, t, J=8.7 Hz, $2\times CH_3CH_2CO$), 1.04 (3H, t, J=7.3 Hz, $CH_3CH_2C{=}C$), 1.47 (4H, t, J=8.7 Hz, $2\times CH_3CH_2CO$), 2.13 (2H, t, J=7.3 Hz, $CH_3CH_2C{=}C$), 2.19 (2H, s, $C{=}CCH_2CO$), and 4.81, 4.92 (2H, 2s, $H_2C{=}C$); δ_C 8.05 ($2\times CH_3CH_2CO$), 12.55 ($CH_3CH_2C{=}C$), 30.96 ($CH_3CH_2C{=}C$, $2\times CH_3CH_2CO$), 44.7 ($C{=}CCH_2O$), 74.35 (CO), 112.35 ($H_2C{=}C$), and 148.5 ($C{=}CH_2$); *m*/*z* 141 (M^+-15, <1%), 57 (81), 55 (23), and 43 (100); HRMS calcd for $C_{10}H_{20}O$ 156.1514, (M^+-CH_3) 141.1279, found 141.1290.

3-Ethyl-5-pentylhex-5-en-3-ol (5i). Colourless oil; t_r 10.89; R_f 0.42 (hexane/ethyl acetate 5:1); ν (film) 3493 (OH), 3074, 1637 (C=CH), and 975 cm^{-1} (CO); δ_H 0.88 (9H, m, J=7.3 Hz, $3\times CH_3$), 1.26–1.40 [6H, m, $(CH_2)_3CH_3$], 1.47 (4H, q, J=7.3 Hz, $2\times CH_3CH_2CO$), 2.10 [2H, t, J=6.9 Hz, $CH_2(CH_2)_3CH_3$], 2.17 (2H, s, $C{=}CCH_2CO$) 4.81, and 4.92 (2H, 2s, $H_2C{=}C$); δ_C 8.10 ($2\times CH_3CH_2CO$), 14.05 [$CH_3(CH_2)_4$], 22.6, 23.4, 29.7, 30.95 [$2\times CH_3CH_2CO$, $(CH_2)_3CH_3$], 38.00, 44.35 [$C{=}CCH_2CO$, $CH_2(CH_2)_3CH_3$], 74.35 (CO), 113.35 ($H_2C{=}C$), and 147.1 ($C{=}CH_2$); *m*/*z* 169 (M^+-29, <5%), 112 (10), 87 (100), 57 (86), 55 (21), and 43 (25); HRMS calcd for $C_{13}H_{26}O$ 198.1984, ($M^{+}+1$) 199.2062, found 199.2084.

1-[2-(1-Hydroxycyclopentylmethyl)allyl]cyclohexan-1-ol (5j). Colourless crystals; mp 57–59°C; t_r 15.05; R_f 0.10 (hexane/ethyl acetate 5:1); ν (KBr) 3332 (OH), 3071, 1632 ($C{=}CH$), and 1055 cm^{-1} (CO); δ_H 1.23–1.33, 1.38–1.64, 1.68–1.85 [18H, 3m, $(CH_2)_5$, $(CH_2)_4$], 2.37, 2.49 (4H, 2s, $2\times CH_2C{=}C$), 4.92, 4.96 (2H, 2s, $H_2C{=}C$); δ_C 22.35, 23.4, 25.7, 38.1, 38.15, 39.95 ($11\times CH_2$), 71.55, 81.7 ($2\times CO$), 117.35 ($H_2\mathit{C}{=}C$), and 144.1 ($\mathit{C}{=}CH_2$); *m/z* 203 ($M^{+}-35$, <1%), 99 (55), 85 (19), 55 (88), and 44 (100); HRMS calcd for $C_{15}H_{26}O_2$ 238.1933, ($M^{+}-H_2O$) 220.1827, found 220.1824.

1-[2-(2-Anilino-2-phenylethyl)allyl]cyclohexan-1-ol (5k). Brown oil; t_r 22.67; R_f 0.28 (hexane/ethyl acetate 5:1); ν (film) 3521 (OH), 3420 (NH), 3055, 3026, 1603, 1504 ($C{=}CH$), and 1045 cm^{-1} (CO); δ_H 1.22–1.64 [10H, m, $(CH_2)_5$], 2.11, 2.20 (2H, AB system, J_{AB}=14.0 Hz, $C{=}C\mathit{CH}_2CO$), 2.44, 2.74 (2H, 2dd, J=14.3, 10.1 and 14.3, 3.9 Hz, CH_2CN), 4.44 (1H, dd, J=10.1, 3.9 Hz, HCN), 6.17, 6.18 (2H, 2s, $H_2C{=}C$), and 6.45–6.62, 7.00–7.38 (10H, m, ArH); δ_C 22.15, 22.2, 25.5, 37.25, 38.4 [$(CH_2)_5$], 47.5 ($\mathit{C}H_2CH$), 56.2 ($C{=}C\mathit{C}H_2CO$), 71.45 (CN), 73.25 (CO), 117.3 ($H_2\mathit{C}{=}C$), 116.95, 117.0, 125.1, 126.0, 126.65, 128.4, 128.45, 128.8, 130.95, 136.75, 143.4, 144.35, 147.5 ($12\times$ArC, $\mathit{C}{=}CH_2$); *m/z* 317 ($M^{+}-18$, 1%), 182 (100), 77 (37), 55 (12); HRMS calcd for $C_{23}H_{29}NO$ 335.2249, found 335.2279.

4-[2-(1-Hydroxycyclohexylmethyl)allyl]tetrahydro-2H-pyran-4-ol (5l). Colourless oil; t_r 16.16; R_f 0.57 (ethyl acetate); ν (film) 3449 (OH), 3048, 1637 ($C{=}CH$),1117, 1026, 996 cm^{-1} (CO); δ_H 1.17–1.68 (14H, m, $(CH_2)_5$, $2\times C\mathit{H}_2CH_2O$), 2.33, 2.61 (4H, 2s, $2\times CH_2C{=}C$), 3.61–3.75 (4H, m, $2\times CH_2O$), 4.87, 4.88 (2H, 2s, $H_2C{=}C$); δ_C 22.3, 25.45, 38.0, 38.3 [$(CH_2)_5$, $2\times \mathit{C}H_2CH_2O$], 37.85, 49.3 ($2\times \mathit{C}H_2C{=}C$), 63.9 ($2\times CH_2O$), 68.4, 71.95 ($2\times CO$), 118.25 ($H_2\mathit{C}{=}C$), and 142.2 ($\mathit{C}{=}CH_2$); *m/z* 255 ($M^{+}+1$, <1%), 101 (100), 83 (18), 71 (87), and 55 (36); HRMS calcd for $C_{15}H_{26}O_3$ 254.1882, found 254.1908.

1-[2-(2-Hydroxy-2-phenylpropyl)allyl]cyclohexan-1-ol (5m). Colourless oil; t_r 15.06; R_f 0.17 (hexane/ethyl acetate 5:1); ν (film): 3360 (OH), 3093, 3070, 3020, 1625, 1601 ($C{=}CH$), and 1070 cm^{-1} (CO); δ_H 1.23–1.62 [10H, m, $(CH_2)_5$], 1.55 (3H, s, CH_3), 2.09, 2.10 (4H, 2s, $2\times CH_2C{=}C$), 4.87, 4.88 (2H, s, $H_2C{=}C$), 7.19–7.35, and 7.43–7.45 (5H, 2m, ArH); δ_C 22.3, 22.35, 25.6, 38.0, 38.4 ($7\times CH_2$), 30.3 (CH_3), 71.75, 74.05 ($2\times CO$), 118.75 ($H_2\mathit{C}{=}C$) and 124.85, 126.4, 128.0, 143.1, 144.1 ($6\times$ArC, $\mathit{C}{=}CH_2$); *m/z* 241 ($M^{+}-33$, 4%), 143 (98), 105 (46), 91 (34), 77 (44), 55 (50), 44 (84), and 43 (100); HRMS calcd for $C_{18}H_{26}O$ 274.1933, ($M^{+}-H_2O-CH_3$) 241.1592, found 241.1576.

Preparation of compounds 6a and 6b
General procedure

A green suspension composed of lithium powder (100 mg, 14 mmol), naphthalene (25 mg, 0.2 mmol), and THF (6 ml) was cooled to −78°C. Then, a solution of chloroether **4** (329 mg, 2 mmol) and the corresponding electrophile (1.98 mmol) in THF (6 ml) was added dropwise for 1.5 h. The mixture was stirred for 30 min at that temperature and then it was hydrolysed with water (10 ml), extracted with ethyl acetate (3×15 ml), and the organic phase was dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure (15 Torr), the resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield compounds **6a** and **6b**. Their physical and spectroscopic data follow:

3-Ethyl-5-(2-methoxyethoxymethyl)hex-5-en-3-ol (6a). Yellow oil; t_r 12.15; R_f 0.24 (hexane/ethyl acetate 5:1); ν (film) 3460 (OH), 3073, 1649 ($C{=}CH$), and 910 cm^{-1} (CO); δ_H 0.82 (6H, t, J=7.3 Hz, $2\times C\mathit{H}_3CH_2$), 1.44 (4H, q, J=7.3 Hz, $2\times C\mathit{H}_2CH_3$), 2.28 (2H, s, $C{=}CCH_2CO$), 3.29 (1H, br s, OH), 3.35 (3H, s, CH_3O), 3.50–3.59 (4H, m, $OC\mathit{H}_2C\mathit{H}_2O$), 4.01 (2H, s, $C{=}CCH_2O$), 5.20, and 5.25 (2H, 2s, $H_2C{=}C$); δ_C 8.05 ($2\times \mathit{C}H_3CH_2$), 30.85 ($2\times \mathit{C}H_2CH_3$), 43.95 ($C{=}C\mathit{C}H_2CO$), 59.0 ($CH_3O$), 69.5, 71.7 ($O\mathit{C}H_2\mathit{C}H_2O$), 73.75 (COH), 75.8 ($C{=}C\mathit{C}H_2O$), 117.8 ($H_2\mathit{C}{=}C$), and 142.45 ($\mathit{C}{=}CH_2$); *m/z* 198 ($M^{+}-18$, 1%), 111 (64), 87 (63), 59 (100), 57 (93), 55 (40), 54 (38), and 45 (91); HRMS calcd for $C_{12}H_{24}O_3$ 216.1725, ($M^{+}-H_2O$) 198.1620, found 198.1653.

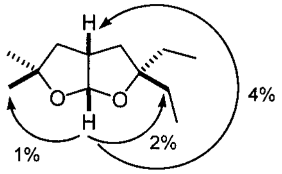
1-[2-(Methoxyethoxymethyl)allyl]cyclopentan-1-ol (6b). Yellow oil; t_r 12.15; R_f 0.23 (hexane/ethyl acetate 5:1); ν (film) 3469 (OH), 3073, 1649 ($C{=}CH$), 1112, and 1058 cm^{-1} (CO); δ_H 1.58–2.10 [8H, m, $(CH_2)_4$], 2.42 (2H, s, $C{=}CCH_2CO$), 3.26 (1H, br s, OH), 3.38 (3H, s, CH_3O), 3.54–3.62 (4H, m, $OC\mathit{H}_2C\mathit{H}_2O$), 4.04 (2H, s, $C{=}CCH_2O$), 5.15 and 5.16 (2H, 2s, $H_2C{=}C$); δ_C 23.65, 39.8 [$(CH_2)_4$], 46.35 ($C{=}C\mathit{C}H_2CO$), 69.3 (CH_3O), 69.3, 71.6 ($O\mathit{C}H_2\mathit{C}H_2O$), 75.55 ($C{=}C\mathit{C}H_2O$), 80.88 (COH), 117.75 ($H_2\mathit{C}{=}C$), and 142.9 ($\mathit{C}{=}CH_2$); *m/z* 196 ($M^{+}-18$, 3%), 59 (100), 55 (39), and 54 (14); HRMS calcd for $C_{12}H_{22}O_3$ 214.1569, ($M^{+}-H_2O$) 196.1463, found 196.1469.

Preparation of the perhydrofuro[2,3-*b*]furans 7

The diols **5** were subjected to tandem hydroboration–oxidation as reported for diols **2**. Compound **7a** was obtained by oxidation of the triol derived from **5a** with $RuCl_2(Ph_3P)_3$ following the same procedure as described for compounds **3a** and **3b**. The rest of the triols were oxidised with PCC, as described for compounds **3c–g**, **3j**, and **3k**, to yield the expected products **7b–d**, **7j**, **7l**, and **7m**. The physical and spectroscopic data of compounds **7** follow:

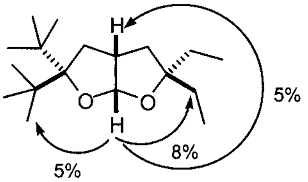
(3a*R**,5*R****,6a*S****) and (3a*R****,5*S****,6a*S****)-5-(*tert*-Butyl)-2,2-diethylperhydrofuro[2,3-*b*]furan** (**7a**, *mixture of diastereoisomers*): colourless oil; t_r 11.75, 11.89; R_f 0.31 (hexane/ethyl acetate 5:1); ν (film) 1100 and 1031 cm^{-1} (CO); δ_H 0.85, 0.86 (12H, 2t, J=7.7, 7.6 Hz, $4\times C\mathit{H}_3CH_2$), 0.89, 0.93 [18H, 2s, $2\times (CH_3)_3C$], 1.57–2.00 (16H, m, $4\times C\mathit{H}_2CH_3$, $4\times C\mathit{H}_2CH$), 2.78, 2.87 (2H, 2m, $2\times CH_2\mathit{CH}CH_2$); 3.59, 3.80 (2H, 2dd, J=11.0, 5.0 and 10.4 Hz, 6.0, $2\times CH_2C\mathit{H}O$); 5.51, and 5.61 (2H, 2d, J=5.5, 5.2 Hz, $2\times OCHO$); δ_C 8.35, 8.8, 8.85 ($4\times \mathit{C}H_3CH_2$); 25.75, 25.85 [$2\times (\mathit{C}H_3)_3C$], 30.5, 31.05, 31.4, 31.95 ($4\times \mathit{C}H_2CH_3$), 32.8, 33.0, 33.2, 33.35 ($4\times C\mathit{H}_2CH$), 39.95, 40.2 ($2\times CH_2\mathit{C}HCH_2$), 43.3 [$2\times C(CH_3)_3$], 76.95 ($2\times COCH_2CH_3$), 85.0, 87.35 [$2\times CHC(CH_3)_3$], 108.7, and 108.85 ($2\times OCO$); *m/z* ($t_r$ 11.75) 197 (M^+-29, 22%), 169 (29), 107 (57), and 57 (100); *m/z* (t_r 11.89) 197 (M^+-29, 22%), 169 (26), 107 (60), and 57 (100); HRMS calcd for $C_{14}H_{26}O_2$ 226.1933, found 226.1950.

(3a*R,6a*S**)-2,2-Diethyl-5,5-dimethylperhydrofuro[2,3-*b*]furan (7b).** Colourless oil; t_r 10.27; R_f 0.38 (hexane/ethyl acetate 4:1); ν (film) 1094 and 1024 cm^{-1} (CO); δ_H 0.84, 0.89 (6H, 2t, J=7.6 Hz, $2\times CH_3CH_2$), 1.20, 1.41 (6H, 2s, $2\times CH_3CO$), 1.44, 1.75 (4H, 2q, J=7.6 Hz, $2\times CH_2CH_3$), 1.64, 1.98 (4H, 2m, $2\times CH_2CH$), 2.93 (1H, m, $CHCH_2$), and 5.63 (1H, d, J=5.7 Hz, OCHO); δ_C 8.2, 8.9 ($2\times CH_3CH_2$), 29.5, 29.55 ($2\times CH_3CO$), 30.45, 31.4 ($2\times CH_2CH_3$), 41.9 ($H_2CCCH_2CH_3$), 44.1 ($CHCH_2$), 44.95 (CH_2CCH_3), 83.15 ($COCH_2$), 88.7 ($COCH_3$), and 109.1 (OCO); *m/z* 183 (M^+-15, <1%), 169 (35), 151 (10), 123 (10), 57 (100); HRMS calcd for $C_{12}H_{22}O_2$ 198.1620, ($M^+-C_2H_5$) 169.1229, found 169.1231.

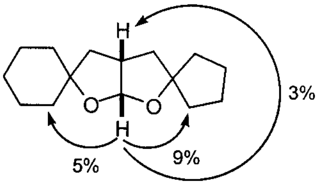


(2*R,3a*S**,6a*R**) and (2*S**,3a*S**,6a*R**)-2-(*tert*-Butyl)-5,5-diethyl-2-methylperhydrofuro[2,3-*b*]furan** (**7c**, *mixture of diasteroisomers*): colourless crystals; mp 154°C; t_r 12.73, 12.83; R_f 0.21 (hexane/ethyl acetate 5:1); ν (film) 1091 and 1019 cm^{-1} (CO); δ_H 0.83, 0.94 (12H, m, $4\times CH_3CH_2$), 0.85, 0.97 [18H, 2s, $2\times (CH_3)_3C$], 1.12, 1.25 (6H, 2s, $2\times CH_3CO$), 1.40–1.79 (16H, m, $4\times CH_2CH_3$, $4\times CH_2CH$), 2.74–2.92 (2H, m, $2\times CHCH_2$); 5.60, and 5.62 (2H, 2d, J=5.5 Hz, $2\times OCHO$); δ_C 8.15, 8.3, 8.85, 8.95 ($4\times CH_3CH_2$), 22.25 ($2\times COCH_3$), 25.44, 25.8 [$2\times (CH_3)_3C$], 30.6, 31.4, 31.6, 32.0 ($4\times CH_2CH_3$), 36.4, 38.1[$2\times C(CH_3)_3$], 38.05, 39.4, 39.9, 40.0 ($4\times CH_2CH$), 43.1, 44.65 ($2\times CHCH_2$), 87.85, 88.9, 91.05, 91.5 ($2\times COCH_2CH_3$, $2\times COCH_3$), 108.5, 110.2 ($2\times OCO$); *m/z* (t_r 12.73) 225 (M^+-15, 2%), 211 (21), 183 (27), 57 (100), and 43 (76); *m/z* (t_r 12.83) 225 (M^+-15, 1%), 211 (20), 183 (36), 165 (11), 57 (100), and 43 (91); HRMS calcd for $C_{15}H_{28}O_2$ 240.2089, (M^++1) 241.2168, found 241.2158.

(3a*R,6a*S**)-2,2-Di(*tert*-butyl)-5,5-diethylperhydrofuro[2,3-*b*]furan (7d).** Colourless oil; t_r 15.14; R_f 0.29 (hexane/diethyl ether 5:1); ν (film) 1109 and 1033 cm^{-1} (CO); δ_H 0.86 (6H, t, J=7.5 Hz, $2\times CH_3CH_2$), 1.10 [18H, s, $2\times (CH_3)_3C$], 1.18–1.84, 1.93–2.25 (8H, 2m, $2\times CH_2CH_3$, $2\times CH_2CH$), 2.90 (1H, m, $CHCH_2$), and 5.71 (1H, d, J=8.1 Hz, OCHO); δ_C 7.95 ($2\times CH_3CH_2$), 28.95 [$2\times (CH_3)_3C$], 29.15, 29.4, 40.4, 42.0 ($4\times CH_2$), 38.6 [$2\times C(CH_3)_3$], 43.4 ($CHCH_2$), 73.1, 82.15 ($2\times CH_2CO$), and 111.15 (OCO); *m/z* 264 (M^+-18, <1%), 107 (16), 57 (100), and 55 (15); HRMS calcd for $C_{18}H_{34}O_2$ 282.2559, ($M^+-C_4H_9$) 225.1854, found 225.1853.



(3a*R,6a*S**)-Dispiro[cyclohexane-1,2′-perhydrofuro[2,3-*b*]furan-5′,1″-cyclopentane] (7j).** Colourless oil; t_r 14.56; R_f 0.81 (hexane/ethyl acetate 4:1); ν (film) 1018 cm^{-1} (CO); δ_H 1.20–1.80, 1.95–2.14 (22H, m, $11\times CH_2$), 2.94 (1H, m, $CHCH_2$), and 5.63 (1H, d, J=5.2 Hz, OCHO); δ_C 23.3, 23.5, 23.75, 24.35, 25.55, 37.4, 38.5, 39.1, 39.9, 42.65 ($11\times CH_2$), 43.4 ($2\times CHCH_2$), 73.35, 85.05 ($2\times COCH_2$), and 108.15 (OCO); *m/z* 236 (M^+, 20%), 207 (20), 55 (66), and 41 (100); HRMS calcd for $C_{15}H_{24}O_2$ 236.1776, found 236.1770.



(3a*R,6a*S**)-Dispiro[cyclohexane-1,2′-perhydrofuro[2,3-*b*]furan-5′,4″-1″-oxacyclohexane] (7l).** Colourless oil; t_r 14.32; R_f 0.17 (hexane/ethyl acetate 5:1); ν (film)1105 and 1031 cm^{-1} (CO); δ_H 1.23–2.05 [18H, m, $(CH_2)_5$, $2\times CH_2CH$, $2\times CH_2CH_2O$], 2.90–2.99 (1H, m, $CHCH_2$), 3.60–3.67, 3.74–3.89 (4H, 2m, $2\times CH_2O$), and 5.66 (1H, d, J=5.5 Hz, OCHO); δ_C 23.25, 23.65, 25.4, 37.85, 38.3, 38.75, 38.8 [$(CH_2)_5$, $2\times CH_2CH_2O$], 42.75 ($CHCH_2$), 43.0, 43.9 ($2\times CH_2CH$), 64.9, 65.15 ($2\times CH_2O$), 81.95, 85.4 ($2\times COCH_2CH$), and 108.35 (OCO); *m/z* 254 (M^++2, <1%), 253 (M^++1, 7%), 252 (M^+, 39%), 223 (20), 110 (12), 55 (86), and 41 (100); HRMS calcd for $C_{15}H_{24}O_3$ 252.1725, found 252.1725.

(2*R,3a*R**,6a*S**) and (2*S**,3a*R**,6a*S**)-2-Phenyl-2-methyl-perhydrofuro[2,3-*b*]furan-5-spiro-1′-cyclohexane** (**7m**, *mixture of diastereoisomers*): colourless oil; t_r 16.18, 16.72; R_f 0.72 (hexane/ethyl acetate 4:1); ν (film) 1010 cm^{-1} (CO); δ_H 1.12–2.00 [20H, m, $2\times (CH_2)_5$], 1.63 (6H, 2s, $2\times CH_3$), 1.77, 2.04, 2.26, 2.61 (8H, 4br s, $4\times CH_2CH$), 2.73, 3.03 (2H, 2m, $2\times CHCH_2$), 5.71, 5.86 (2H, 2d, J=5.2, 5.5 Hz, $2\times OCHO$), and 7.19–7.51 (10H, m, ArH); δ_C 23.35, 23.4, 23.55, 23.7, 25.45 [$2\times (CH_2)_5$], 25.4 ($2\times CH_3$), 38.5, 38.75, 44.95, 46.1 ($4\times CH_2CH$), 43.35, 43.75 ($2\times CHCH_2$), 85.65, 86.3 ($4\times COCH_2$), 108.65, 108.95 ($2\times OCO$), 124.35, 125.15, 126.2, 126.35, 127.65, 128.1, 148.1, 148.15 ($12\times ArC$); *m/z* (t_r 16.18) 273 (M^++1, 5%), 272 (M^+, 27%), 257 (53), 91 (45), 77 (36), and 43 (100); *m/z* (t_r 16.72) 273 (M^++1, 5%), 272 (M^+, 22%), 257 (64), 105 (71), 91 (45), 77 (36), and 43 (100); HRMS calcd for $C_{18}H_{24}O_2$ 272.1776, found 272.1794 and 272.1793.

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