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Rearrangement of Allyl Aryl Ethers III[1] Reaction of Alkoxyhydroquinone with Cycloalkenediols

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Abstract: Cycloalkenobezofurans **5a-d** were prepared in one-pot reaction from methoxyhydroquinone, 2,6- and 2,3-dialkoxyhydroquinone (**1**) with cycloalkenediol (**2**). Reaction between the isomeric 2,5-dialkoxyhydroquinones (**9**) with diol **2** led to the formation of monoalkoxybenzofurans **5d-g** with the loss of an alkoxy group. © 1997 Elsevier Science Ltd.

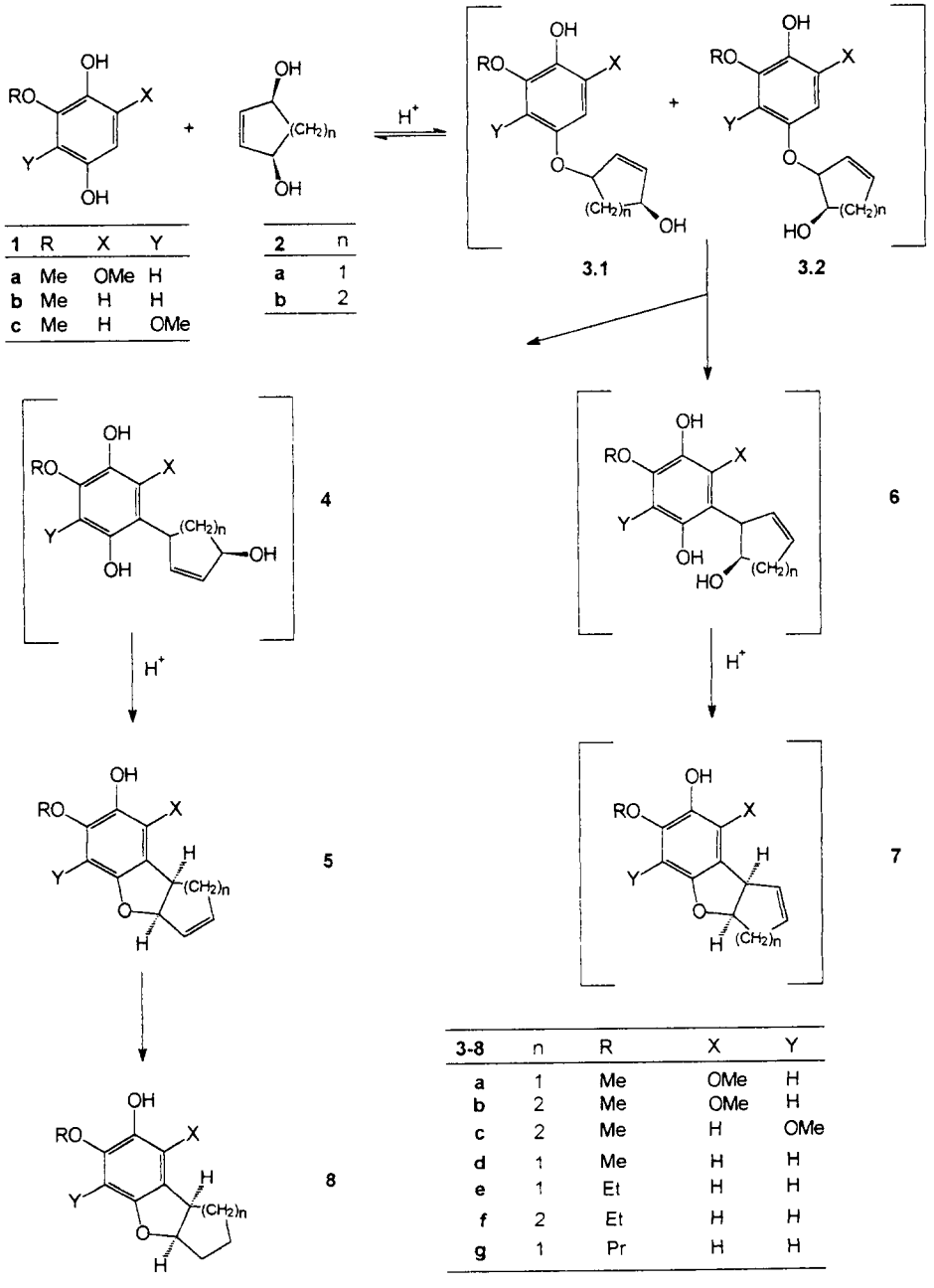
We have recently established a convenient one-pot synthetic method for the preparation of benzofuran derivatives *via* reaction of alkylhydroquinones with alkenediol and cycloalkenediols[1-3]. As an extension of this research, we have examined the reaction of alkoxyhydroquinones (**1**) with cycloalkenediols (**2**). The variation of the substituents of hydroquinones could prove the general applicability of this new method and also be a convenient route to obtain alkoxybenzofurans.

The hydroquinones with methoxy groups in positions 2 and 6 (Scheme 1, **1a**) reacted smoothly with either cyclopent-4-ene-1,3-diol (**2a**) or cyclohex-2-ene-1,4-diol (**2b**) in the presence of catalytic amounts of 10-camphorsulfonic acid and afforded benzofurans **5a** and **5b** (respectively). The same type of reaction was observed between the 2,3-dimethoxyhydroquinone (**1c**) and **2b**, and compound **5c** was isolated in moderate yield. Although we could not isolate structure isomers **7a-c**, their presence in the crude products was shown by HPLC. The amounts of **7a-c** did not exceed 5% and were eliminated during purification.

The above reactions apparently proceeded by similar sequence of events as we had postulated for alkylhydroquinones. Namely, initial acid-catalyzed formation of ethers **3.1** and **3.2**, followed by 1,3- and/or 3,3-sigmatropic rearrangements[4]. The resultant hydroquinones **4** and **6** then underwent acid-catalyzed cyclization to afford benzofurans **5** and **7**, respectively.

An alternative mechanism for the formation of intermediates **4** and **6** may be direct electrophilic substitution reaction between the hydroquinone **1** and a cation formed from the diol **2**.

Having examined the reactions of positional isomers **1a** and **1c**, it was next of interest to react the 2,5-dialkoxyhydroquinones **9** with diol **2** (Scheme 2). Here, the acid-catalyzed reaction between 2,5-dimethoxy-hydroquinone (**9a**) and cis-4-cyclopentene-1,3-diol (**2a**) was rather fast and afforded unexpected product. ^{1}H and ^{13}C NMR analyses (Experimental) showed that one of the methoxy groups of the starting material



1	R	X	Y
a	Me	OMe	H
b	Me	H	H
c	Me	H	OMe

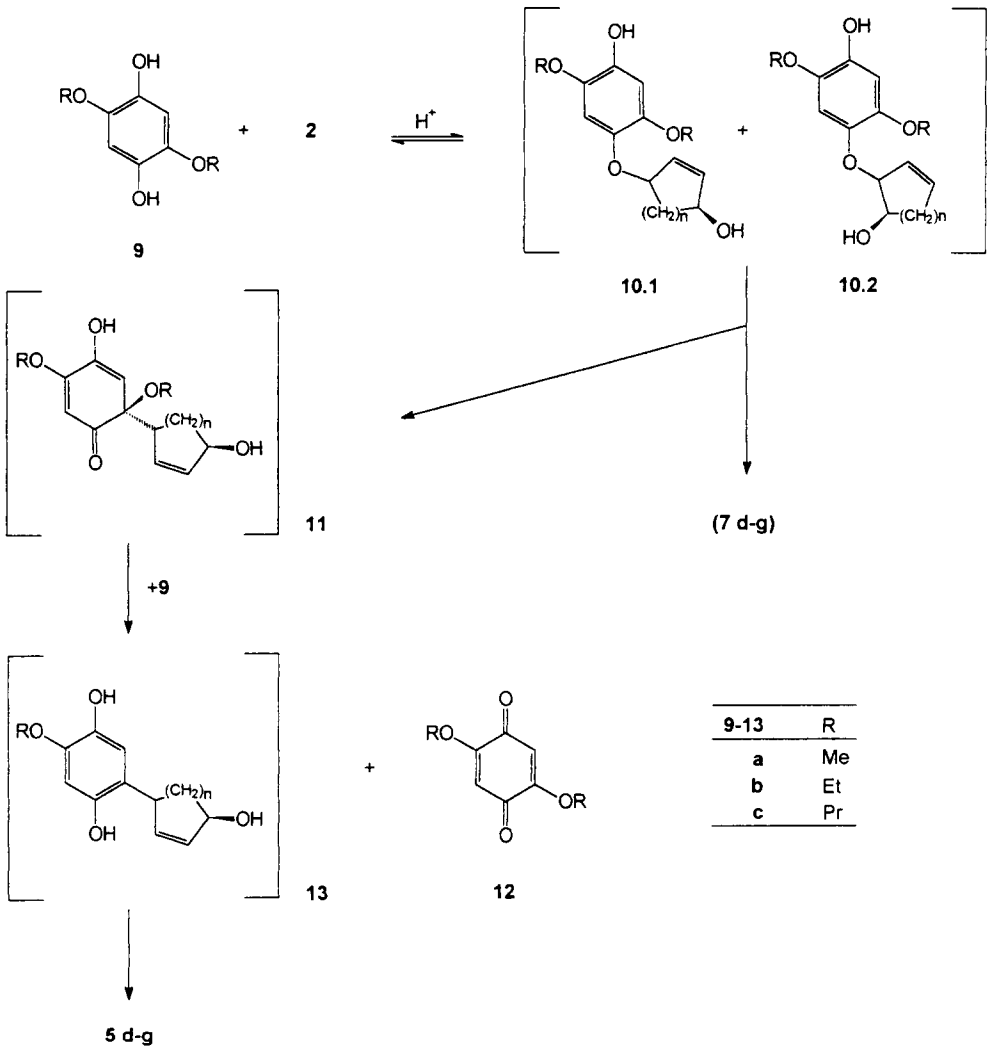
2	n
a	1
b	2

3-8	n	R	X	Y
a	1	Me	OMe	H
b	2	Me	OMe	H
c	2	Me	H	OMe
d	1	Me	H	H
e	1	Et	H	H
f	2	Et	H	H
g	1	Pr	H	H

Scheme 1.

was eliminated in the reaction and compound **5d** was formed. Besides this product 2,5-dimethoxybenzoquinone (**12a**) was also isolated. The amount of the latter (0.5 equiv.) showed that approximately half of the starting hydroquinone was oxidized to its corresponding quinone (**12a**).

In order to confirm the structure of **5d**, we also treated the methoxyhydroquinone (**1b**) with diol **2a**. The reaction was performed under the same condition as in the case of dialkoxy compound (**9a**) and afforded **5d** in acceptable yield.



9-13	R
a	Me
b	Et
c	Pr

Scheme 2.

The reactions between the homologues **9b** and **9c**, and diol **2** gave the same results. In all cases, one of the alkoxy groups had been lost and besides monoalkoxybenzofurans (**5e-g**), their corresponding benzoquinones (**12b,c**) were isolated.

These reactions leading to monoalkoxybenzofurans (**5d-g**) would also likely involve the initial acid-catalyzed formation of ethers (**10.1** and **10.2**) followed by 1,3- and/or 3,3-sigmatropic migrations. The resulting intermediate **11** is then reduced by the unchanged starting hydroquinone **9** to furnish monoalkoxyhydroquinone **13**. Acid-catalyzed intramolecular cyclization with allylic rearrangement of the latter affords the products **5d-g**.

An alternate mechanism for the formations of intermediates **11** and **13** may be direct electrophilic attack at the position bearing the methoxy group (generally called the ipso position)[5] followed by the required reduction step.

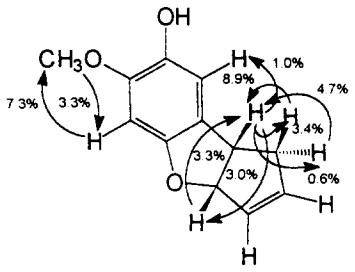
These new compounds **5a-g** were smoothly hydrogenated to their partially saturated analogs **8a-g** using 10% palladium on charcoal catalyst.

Establishment of the structure of **5** and **8** including stereochemistry and regiochemistry was made by extensive ^{1}H and ^{13}C NMR studies. For example, cis-fused stereostructure of **5d** was established by differential nuclear Overhauser enhancement experiments. Thus, irradiation of 3-H resulted in the enhancement of 2-H (3%), 3'-H_{β} (3.4%), and 4-H (1.0%). Irradiation of 2-H resulted in enhancement of the signal for 3-H (3.3%). Comparing the selected N.O.E. data (Scheme 3) to the data of similar cis-fused benzofurans published by us[1], we assumed cis-fused stereostructure for compounds **5a-g** and **8a-g**.

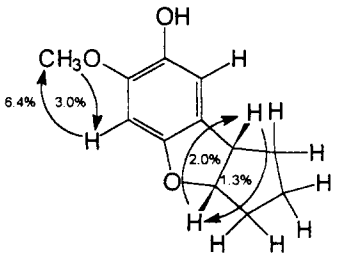
In summary, acid-catalyzed reactions of methoxyhydroquinone, 2,6- and 2,3-dialkoxyhydroquinones (**1**) with cycloalkenediol (**2**) afforded cycloalkenobenzofurans **5a-d** in one operation. However, the reaction between the isomeric 2,5-dialkoxyhydroquinone (**9**) and cycloalkenediol (**2**) yielded monoalkoxy-benzofurans (**5d-g**) with the elimination of one methoxy group. These novel one-pot procedures for the preparations of alkoxybenzofurans promise to have wide application in syntheses. All new compounds are of potential biological interest.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded on Spekord IR 20 M spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker DRX-500 spectrometer internal standard TMS. The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), sextet (sext), multiplet (m), and broad (br). MS measurements were carried out with a Kratos MS-25 RFA combined GC/MS system. Only selected peaks from infrared and mass spectra are quoted. HPLC chromatographic analyses were performed with a Waters 600 equipped with a photodiode array detector 990. Stationary phase: Waters C-18 (150x4.6 mm). Merck precoated silica gel 60 F_{254} plates were used for thin-layer chromatography and Kieselgel® 60 for column chromatography. All solvents were dried by means of standard methods.



5d



8a

Compound	Irradiate	Observe	N.O.E. (%)
5d	C3-H	C2-H	3.0
		C3'-H_β	3.4
	C2-H	C3-H	3.3
	OCH_3	C7-H	3.3
	C7-H	OCH_3	7.3
5d benzoate	C3-H	C2-H	7.1
		C3'-H_β	4.2
	C2-H	C3-H	3.3
	OCH_3	C7-H	4.4
	C7-H	OCH_3	8.7
8d benzoate	C3-H	C2-H	7.3
	C2-H	C3-H	6.9
8a	C3-H	C2-H	1.3
	C2-H	C3-H	2.0
	OCH_3	C7-H	3.0
	C7-H	OCH_3	6.4

Scheme 3. Some N.O.E. assignments of selected benzofurans.

cis-5-Hydroxy-4,6-dimethoxy-2,3-(2-cyclopenteno)-2,3-dihydrobenzofuran (5a). To a stirred mixture of **1a** (5.0 g, 29 mmol)[6] and **2a** (3,5 g, 29 mmol)[7] in dry toluene (30 ml) was added (1R)-(-)-10-camphorsulfonic acid monohydrate and the resultant solution was stirred at 70°C for 3 h under argon. After cooling, the reaction mixture was diluted with EtOAc and washed successively with water and brine, and then dried ($MgSO_4$). Evaporation of the solvent in vacuo gave a syrup which was purified with hexane/acetone (10:1, v/v) as eluent to yield **5a** (2,3 g, 33.9%, yellow solid). M.p.: 140°C (hexane); TLC: R_f= 0.32 (hexane/acetone, 5:2, v/v); IR (KBr): 3520, 3480, 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.67 and 2.85

(2H, m, CH_2), 3.81 (3H, s, OCH_3), 3.97 (3H, s, OCH_3), 4.16 (1H, dd, J= 8 and 2.5 Hz, CH), 5.11 (1H, br.s, OH), 5.79 (1H, m, CH-O), 5.84 (1H, m, CH=), 6.03 (1H, m, =CH), 6.18 (1H, s, aromatic-H); ^{13}C NMR ($CDCl_3$): δ = 39.60(C-3'), 42.47 (C-3), 56.57 (CH_3-O), 59.90 (CH_3O), 89.70 (C-2), 92.97 (C-7), 113.64 (C-3a), 129.13 (C-2'), 131.55 (C-5), 135.70 (C-1'), 143.60 (C-6), 147.72 (C-4), 151.46 (C-7a); MS [*m/z* (relative intensity %]: 234 (M^+; 100), 219 (28), 207 (13), 193 (7), 169 (6), 131 (7); Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02 Found: C, 66.51, H, 6,18.

cis-2-Hydroxy-1,3-dimethoxy-5a,8,9,9a-tetrahydrodibenzofuran (**5b**). To a stirred mixture of **1a** (5.0 g, 29 mmol) and **2b** (7.0 g, 61 mmol)[8] in dry toluene (100 ml) was added (1R)-(-)-10-camphorsulfonic acid monohydrate (1.0 g) and the resultant solution was stirred at 70°C for 5 h under argon. After cooling, the reaction mixture was diluted with Et_2O and washed successively with water and brine, and then dried ($MgSO_4$). Evaporation of the solvent in vacuo gave a syrup which was purified by chromatography with hexane /Et_2O (1:1, v/v) as eluent to yield **5b** (2.52 g, 35.0%, yellow oil). TLC : R_f= 0.8 (hexane/Et_2O, 1:1, v/v); IR (nujol): 3420, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.55 (1H, m, CH_2), 1.93 (2H, m, CH_2), 2.09 (1H, m, CH_2), 3.86 (3H, s, OCH_3), 3.97 (3H, s, OCH_3), 4.05 (1H, m, CH), 5.1 (1H, s, OH), 5.8 (1H, m, CH), 5.86 (1H, m, =CH), 6.03 (1H, m, CH=), 6.18 (1H, s, aromatic-H); MS [*m/z* (relative intensity %)]: 248 (M^+, 100), 233 (11), 183 (35), 167 (8); Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.72; H, 6.50 Found: C, 67.91; H, 6.72.

3,4-Dimethoxy-5a,8,9,9a-tetrahydrodibenzofuran-2-ol (**5c**). A mixture of **1c** (3.0 g, 18 mmol)[9], **2b** (2.2 g, 20 mmol) and 0,1 g of (1R)-(-)-10-camphorsulfonic acid monohydrate in toluene (50 ml) was stirred at 70°C for 48 h under argon. Evaporation of the solvent in vacuo afforded a yellow oil which was purified by repeated flash chromatography with hexane/acetone (5:0.2 , v/v) to yield **5c** (0.8 g, 17,9%, light yellow oil).TCL: R_f= 0,5 (hexane/acetone, 5:2, v/v); HPLC: R_t= 12.18 min. (acetonitrile/H_2O, 2.5:7.5, v/v); IR (nujol): 3430, 1600, 1460 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.61 (1H, m, CH_2), 1.94 (2H, m, CH_2), 2.1 (1H, m, CH_2), 3.30 (1H, m, CH), 3.90 (3H, s, CH_3O), 3.97 (3H, s, CH_3O), 4.97 (1H, m-d, J= 7 Hz, CH), 5.37 (1H, br.s, OH), 5.94 (1H, m, CH=), 6.08 (1H, m =CH), 6.51 (1H, s, aromatic-H); ^{13}CNMR: δ = 22.69 (C-9), 25.01 (C-8), 40.47 (C-9a), 60.26 (CH_3O), 61.34 (CH_3O), 79.29 (C-5a), 104.01 (C-1), 124.62 (C-7), 127.34 (C-6), 133.26 (C-5), 137.59 (C-7), 138.18 (C-9b), 143.20 (C-2), 143.64 (C-4a). Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.72; H, 6.50 Found: C, 67.43; H, 6.26.

General Procedure for the Preparation of Alkoxybenzofurans 5d-g. To a stirred suspension of dialkoxyhydroquinone **9** (50 mmol) and the corresponding cycloalkenediol **2** (55 mmol) in dry toluene (100 ml), catalytic amounts of (1R)-(-)-10-camphorsulfonic acid monohydrate (2 mmol) was added. The reaction mixture was stirred at 70°C for the time indicated under argon. After cooling, the precipitated dialkoxybenzoquinone **12** was filtered off and the solvent was evaporated in vacuo. The residue was purified by column chromatography using hexane/acetone (10:5, v/v) as eluent, followed by recrystallization from hexane.

cis-5-Hydroxy-6-methoxy-2,3-(2-cyclopenteno)-2,3-dihydrobenzofuran (**5d**). Following the general procedure, from 2,5-dimethoxyhydroquinone (**9a**)[10] and **2a** with a reaction time 6 hr, **12a**[10,11] and **4d** were isolated (3,7 g, 88,1% and 1,80 g, 35,3%, respectively). **5d** : white prisms; M.p. 116-118°C; TLC : R_f= 0.5 (hexane/acetone, 5:2, v/v); HPLC : R_t= 6.7 min. (hexane/CH_2Cl_2/dioxane, 9:1:0.01, v/v); IR (KBr) : 3450,

1630 cm^{-1}; ^1H NMR ($CDCl_3$) : δ = 2.52 (1H, m-dd, *J*= 16 and 2 Hz, CH_2), 2.86 (1H, m-ddd, *J*= 16,8 and 1 Hz, CH_2), 3.81 (3H, s, OCH_3), 4.00 (1H, m-d, *J*= 8 Hz, CH), 5.25 (1H, br.s, OH), 5.79 (1H, m-d, *J*= 8 Hz, CH-O), 5.82 (1H, m, CH=), 6.00 (1H, m, =CH), 6.38 (1H, s, aromatic-H), 6.72 (1H, s, aromatic-H); ^{13}C NMR ($CDCl_3$): δ = 40.25 (C-3'), 43.52 (C-3), 56.12 (CH_3-O), 92.92 (C-2), 94.28 (C-7), 110.22 (C-4), 122.33 (C-3a), 129.40 (C-2') 135.33 (C-1'), 139.65 (C-5), 146.46 (C-6), 151.37 (C-7a); MS [*m/z* (relative intensity %)] : 204 (M^+; 100), 189 (47), 177 (22), 161 (12), 133 (10), 155 (16); Anal.Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92 Found: C, 70.36; H, 5.69.

Benzoate of 5d. This compound was prepared from **5d** and benzoyl chloride by standard method. M.p. 105°C (colorless needles); TLC : R_f= 0.52 (hexane/acetone, 5:2, v/v); HPLC : R_t= 38.19 min. (acetonitrile/H_2O/H_3PO_4, 4:6:0.05, v/v); IR (KBr): 1730 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.52 (2H, m, CH_2), 3.70 (3H, s, OCH_3), 4.05 (1H, m, CH), 5.72 (1H, m, CH-O), 5.85 (1H, m, CH=), 6.03 (1H, m, =CH), 6.45 (1H, s, aromatic-H), 6.90 (1H, s, aromatic-H), 7.8 (3H, m, aromatic-H), 8.1 (2H, m, aromatic-H); ^{13}C NMR: ($CDCl_3$): δ = 40.34 (C-3'), 43.17 (C-3), 56.12 (CH_3O), 93.87 (C-2) 95.40 (C-7), 118.57 (C-4), 122.42 (C-3a), 128.46 (C-3" and C-5"), 129.29 (C-1'), 129.67 (C-1"), 130.24 (C-2" and C-6"), 133.32 (C-4"), 133.49 (C-5), 135.55 (C-2'), 151.58 (C-7a), 156.92 (C-5), 165.30 (COO).

Acetate of 5d. This compound was prepared from **5d** in 75% by standard procedure. M.p.107°C; TLC : R_f= 0.75 (hexane/acetone, 5:2 v/v); IR (KBr) : 1740, 1620, 1580, 1460, 1200 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.0 8 (3H, s, CH_3), 2.4-2.9 (2H, m, CH_2), 3.78 (3H, s, OCH_3), 3.98 (1H, m, CH), 5.7 (1H, m, CH-O), 5.80 (1H, m, CH=), 5.95 (1H, m, =CH), 6.42 (1H, s, aromatic-H), 8.8 (1H, s, aromatic-H).

cis-6-Ethoxy-5-hydroxy-2,3-(2-cyclopenteno)-2,3-dihydrobenzofuran (**5e**). Following the general procedure, using **9b**[10,13] and **2a**, with a reaction time 30 h, 2.81 g (51.5%) of **4e** and 4.8 g (97.76%) of **12b**[11,12] were isolated, **5e:** white plates; M.p. 94-96°C; TLC: R_f= 0.5 (hexane/acetone, 5:2, v/v); HPLC : R_t= 5.73 min. (acetonitrile/H_2O/H_3PO_4, 4:6:0.05, v/v); IR (KBr): 3400, 1620 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.40 (3H, t, *J*= 6 Hz, CH_3), 2.52 (1H, m-dd, *J*= 16 and 2 Hz, CH_2), 2.86 (1H, m-ddd, *J*= 16, 8, and 1 Hz, CH_2), 4.02 (3H, m, CH and OCH_2), 5.28 (1H, s, OH), 5.79 (1H, m-d, *J*= 8 Hz, CH-O), 5.82 (1H, m, =CH), 6.00 (1H, m, CH=), 6.38 (1H, s, aromatic-H), 6.72 (1H, s, aromatic-H); ^{13}C NMR ($CDCl_3$): δ = 14.85 (CH_3), 40.24 (C-3'), 43.52 (C-3), 64.69 (CH_2O), 92.87 (C-2), 95.08 (C-7), 110.09 (C-4), 122.16 (C-3a), 129.40 (C-2'), 135.23 (C-1'), 139.80 (C-5), 145.63 (C-6), 151.28 (C-7a); MS [*m/z* (relative intensity %)]: 218 (M^+; 100), 189 (47), 163 (28), 133 (11), 115 (16); Anal. Calcd. for $C_{13}H_{14}O_3$: C,. 71.54; H, 6.47 Found C, 71.29; H, 6.62.

cis-3-Ethoxy-5a,8,9,9a-tetrahydrodibenzofuran-2-ol (**5f**).This compound was prepared from **9b** and **2b** following the general procedure, with a reaction time 30 h. Purification yielded **5f** (1.86 g, 32.0%) and **12b**[13] (3.7 g, 75.5%). **5f**: Colorless needles; M.p. 92-94°C; TLC : R_f= 0.52 (hexane/acetone, 5:2, v/v); HPLC : R_t= 2.55 min. (acetonitrile/H_2O, 1:3, v/v); IR (KBr): 3480, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) : δ = 1.40 (3H, t, *J* = 7 Hz, CH_3), 1.55 (1H, m, CH_2), 1.92 (2H, m, CH_2), 2.09 (1H, m, CH_2), 3.31 (1H, m, CH), 4.05 (2H, q, *J*= 7Hz,OCH_2), 4.95 (1H, m, CH), 5.30 (1H, s, OH), 5.93 (1H, m, =CH), 6.11 (1H, m, =CH), 6.40 (1H, s, aromatic-H), 6.77 (1H, s, aromatic-H). Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94 Found C, 72.12; H, 7.05.

cis-5-Hydroxy-6-propyloxy-2,3-(2-cyclopenteno)-2,3-dihydrobenzofuran (5g). Following the general procedure, from **9c**[13] and **2a**, with a reaction time 30 h, **5g** and **12c**[13] were isolated (1.8 g, 30.1% and 3.2 g, 57.0%, respectively). **5g** : colorless needles; M.p. 69°C; TLC : R_f= 0.6 (hexane/acetone, 5:2, v/v); HPLC : R_t= 11.25 min. (acetonitrile/H_2O/H_3PO_4, 4:6:0.15, v/v); IR (KBr): 3400, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) : δ = 1.02 (3H, t, *J*= 6.5 Hz, CH_3), 1.80 (2H, sext., *J*= 6.5 Hz, CH_2), 2.54 (1H, m, *J*= 17, 2.5, 2.5, 2.2 and 2 Hz, CH_2), 2.86 (1H, m, *J*= 17, 7,5, 2.0, 2.0 and 1.3 Hz, CH_2), 3.91 (1H, m, *J*= 9 and 6.5 Hz, OCH_2), 3.94 (1H, m, *J*= 9 and 6.5 Hz, OCH_2), 4.00 (1H, m, *J*= 8, 7.5, 2.9 and 2.0 Hz, CH), 5.28 (1H, s, OH), 5.78 (1H, m, *J*= 8, 2.5, 1.9, 1.8 and 1.3 Hz, CH), 5.82 (1H, m, *J*= 5.5, 2.5, 2.0, 1.8, 0.3 Hz, =CH), 6.00 (1H, m, *J*= 5.5, 2.2, 2.0, 1.9 Hz, =CH), 6.37 (1H, s, aromatic-H), 6.73 (1H, s, aromatic-H). ^{13}C NMR ($CDCl_3$) : δ = 10.75 (CH_3), 22.76 (CH_2), 40.51 (C-3'), 43.80 (C-3), 70.90 (0-CH_2), 93.14 (C-2), 95.38 (C-7), 110.33 (C-4), 122.39 (C-3a), 129.68 (C-2'), 135.48 (C-1'), 140.09 (C-5), 146.01 (C-6), 151.56 (C-7a); Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94 Found: C, 72.20, H, 7.06.

General Procedure for the Preparation of cycloalkanobenzofurans 8a-g. A solution of the appropriate cycloalkenobenzofuran **5** (20 mmol) in dry methanol (200 ml) was shaken in an atmosphere of hydrogen with palladium/charcoal catalyst (1.0 g) for 30 min. The catalyst was removed by filtration and the filtrate was concentrated in vacuo. The residue was purified by recrystallization from hexane.

cis-5-Hydroxy-4,6-dimethoxy-2,3-cyclopentano-2,3-dihydrobenzofuran (8a). Yield 3.6 g (76.2%) colorless crystals. M.p. 125-126°C; TLC : R_f= 0.73 (hexane/acetone, 5:2, v/v); IR (KBr) : 3460, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) : δ = 1.4-2.05 (6H, m, 3 CH_2), 3.80 (3H, s, OCH_3), 3.96 (4H, s+m, OCH_3, CH), 5.0 (1H, br.s, OH), 5.18 (1H, m, CH), 6.13 (1H, s, aromatic-H); ^{13}C NMR ($CDCl_3$): δ = 23.58 (C-2'), 33.65 (C-3'), 35.18 (C1'), 45.47 (C-3), 56.29 (OCH_3), 59.81 (OCH_3), 88.71 (C-7), 89.38 (C-2), 113.23 (C-3a), 131.31 (C-5), 143.36 (C-4), 147.41 (C-6), 153.55 (C-7a). Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.08, H, 6.83 Found: C, 66.17; H, 6.88.

cis-2-Hydroxy-1,3-dimethoxy-5a,6,7,8,9,9a-hexahydrodibenzofuran (8b). Yield 3.4 g (67.9%) light brown solid. M.p. 97-98°C; TLC : R_f= 0.65 (hexane/acetone, 5:2, v/v); IR (KBr) : 3420, 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.2-2.1 (8H, m, 4CH_2), 3.78 (3H, s, OCH_3), 3.91 (1H, m, CH), 3.98 (3H, s, OCH_3), 4.55 (1H, m, CH-O), 5.2 (1H, br.s, OH), 6.18 (1H, s, aromatic-H). Anal. Calcd. for $C_{14}H_{18}O_4$; C, 67.18, H, 7.25 Found C, 67.02, H, 7.44.

cis-5-Hydroxy-6-methoxy-2,3-cyclopentano-2,3-dihydrobenzofuran (8d).Yield 3.4 g (82.4%) colorless needles; M.p. 100-103°C; TLC : R_f= 0.54 (hexane/acetone, 5:2, v/v); HPLC : R_t= 3.84 min. (acetonitrile/H_2O, 4:6, v/v); IR (KBr) : 3400, 1600, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) : δ = 1.49 (1H, m, CH_2), 1.6-1.9 (4H, m, 2CH_2), 2.03 (1H, m, CH_2), 3.76 (1H, m-t, *J*= 8 Hz, CH), 3.81 (3H, s, OCH_3), 5.16 (1H, s, OH), 5.22 (1H, m-t, O-CH), 6.32 (1H, s, aromatic-H), 6.68 (1H, s, aromatic-H); Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84 Found: C, 70.11; H. 6.82.

Benzoate of 8d was prepared in 81% yield by standard procedure. M.p.114°C; TCL : R_f= 0.5 (hexane/acetone, 5:2, v/v (; IR (KBr): 1720, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) : δ = 1.55 (1H, m, CH_2), 1.65-1.9 (4H, m, 2CH_2), 2.07 (1H, m, CH_2), 3.74 (3H, s, CH_3O), 3.82 (1H, m-t, *J*= 8 Hz, CH), 5.3 (1H, m, CH-O), 6.42 (1H, s,

aromatic-H), 6.88 (1H, s, aromatic-H), 7.48 (2H, m, aromatic-H), 7.6 (1H, m, aromatic-H), 8.2 (2H, m, aromatic-H); ^{13} C NMR ($CDCl_3$): δ = 23.56 (C-2'), 34.73 (C-3'), 35.34 (C-1'), 46.45 (C-3), 56.10 (CH_3O), 90.19 (C-2), 94.27 (C-7), 118.43 (C-4), 122.12 (C-3a), 128.45 (C-3" and C-5"), 129.70 (C-1"), 130.22 (C-2" and C-6"), 133.28 (C-4"), 151.20 (C-7a), 159.01 (C-6), 165.30 (COO).

cis-6-Ethoxy-5-hydroxy-2,3-cyclopentano-2,3-dihydrobenzofuran (8e). Yield 2.50 g (56.8%) colorless crystals. M.p. 94-96°C; TLC : R_f= 0.58 (hexane/acetone, 5:2, v/v); IR (KBr): 3420, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) : δ = 1.42 (3H, t, *J*= 6.5 Hz, CH_3), 1.48 (1H, m, CH_2), 1.6-1.9 (4H, m, CH_2), 2.04 (1H, m, CH_2), 3.77 (1H, m-t, *J*= 8 and 2.5 Hz, CH), 4.03 (2H, q, *J*= 6.5 Hz, O-CH_2), 5.22 (1H, m, *J*= 8 Hz, O-CH), 5.26 (1H, s, OH), 6.30 (1H, s, aromatic-H), 6.69 (1H, s, aromatic-H); ^{13}C NMR ($CDCl_3$) : δ = 14.84 (CH_3), 23.50 (C-2'), 34.68 (C-1'), 35.44 (C-3'), 46.80 (C-3), 64.65 (O-CH_2), 89.25 (C-2), 93.91 (C-7), 95.08 (C-4), 110.04 (C-3a), 121.82 (C-5), 139.52 (C-6), 145.17 (C-7a); Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32 Found: C, 71.01; H, 7.57.

Alternate preparation of 5d. (1R)-(-)-10-camphorsulfonic acid monohydrate (0.8 g) was added to a solution of **1b** (11.3 g, 81 mmol)[14] and **2a** (9.38 g, 92 mmol) in dry toluene (110 ml), and the mixture was stirred at 70°C for 16 h, under argon. After cooling, the solvent was removed and the residue extracted several times with CH_2Cl_2. The combined organic extracts were washed successively with water and brine, and then dried ($MgSO_4$). Evaporation of the solvent in vacuo gave a solid which was recrystallized from hexane to afford **5d** (7.94 g, 48%). The spectral data of this compound matched in all aspects the data of **5d** reported above.

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