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Rearrangement of Allyl Aryl Ethers II;[1] Reaction of Hydroquinone with Cycloalkenediols

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Cycloalkenobenzofurans **5** and **7** are prepared in one operation from hydroquinone **1** and cycloalkenediol **2** involving a sequence of acid-catalyzed formation of ether **3**, 1,3- and or 3,3-rearrangements, and acid-catalyzed intramolecular cyclization of **4** and **6** generated as intermediates.

Sigmatropic rearrangement of allyl aryl ethers has been widely used in synthesis for constructing carbon–carbon bonds.[2–6] In the preceding papers we have described the competing 1,3- and 3,3-rearrangements of allyl aryl ethers leading to the formation of 2,3-dihydrobenzofuran-5-ols.[1,7,8] Some representatives of this class of compounds have been shown to be potent inhibitors of leukotriene biosynthesis.[9,10] Continuing our program, we investigated the thermal rearrangement reactions of allyl aryl ethers generated in situ from hydroquinones **1** and cycloalkenediols **2** (Scheme 1).

The reaction between trimethylhydroquinone (**1a**) and *cis*-cyclopent-4-ene-1,3-diol (**2a**)[11] was carried out in anhydrous toluene at 70 °C in the presence of catalytic amounts of 10-camphorsulfonic acid. The reaction was rather slow and yielded a 5:1 mixture of two isomeric compounds **5a** and **7a**. Although we could get pure **5a** by repeated recrystallization of the above mixture, we were unable to obtain **7a** in a pure state. Therefore, this mixture was acylated and the resulting mixture of acetates was separated by repeated chromatography to afford the pure acetate of **7a**. The latter was converted into **7a** by base-catalyzed transesterification.

The structures of compounds **5a** and **7a** were established by ^{1}H and ^{13}C NMR spectroscopy and MS data (see experimental). Further support for the structural assignment was obtained by chemical reactions. Treatment of **5a** with iron(III) chloride in a mixture of alcohol and water afforded the structurally isomeric quinones **9** and **10** (ratio 3:2). Here, the alkoxy group of the products matched the alcohol used as a solvent in the reaction. For instance, when the reaction was performed in methanol/water, the methoxy-substituted quinones **9a** and **10a** were obtained (Scheme 2).

Hydrogenation of a mixture of **5a** and **7a** or the pure **5a** over palladium catalyst yielded the same product, namely **8a**, proving that the two compounds differ only in the position of the carbon-carbon double bond (Scheme 1).

The formation of the isomeric benzofuranols **5a** and **7a** can be interpreted as the result of competing 1,3- and 3,3-rearrangements (Scheme 1). These multistep transformations require the initial acid-catalyzed formation of ether **3**, which in turn undergoes either 1,3- or 3,3-sigmatropic migration. The resulting hydroquinones **4** and **6** cannot be isolated but undergo rapid acid-catalyzed cyclization to afford **5** and **7**, respectively.

The ratio of products **5a** and **7a** was dependent upon reaction temperature. At lower temperature (50 °C), the 1,3-shift was heavily favoured (ratio 5:1) and after recrystallization pure **5a** was isolated. When the reaction was carried out in boiling toluene the 3,3-(Claisen) rearrangement became more competitive and a 3:2 mixture of **5a** and **7a** was obtained.

Due to the acidic condition used, an alternative mechanism for the formation of **5** and **7** may be direct electrophilic substitution reaction between **1** and **2** followed by acid-catalyzed cyclization of intermediates **4** and **6**.

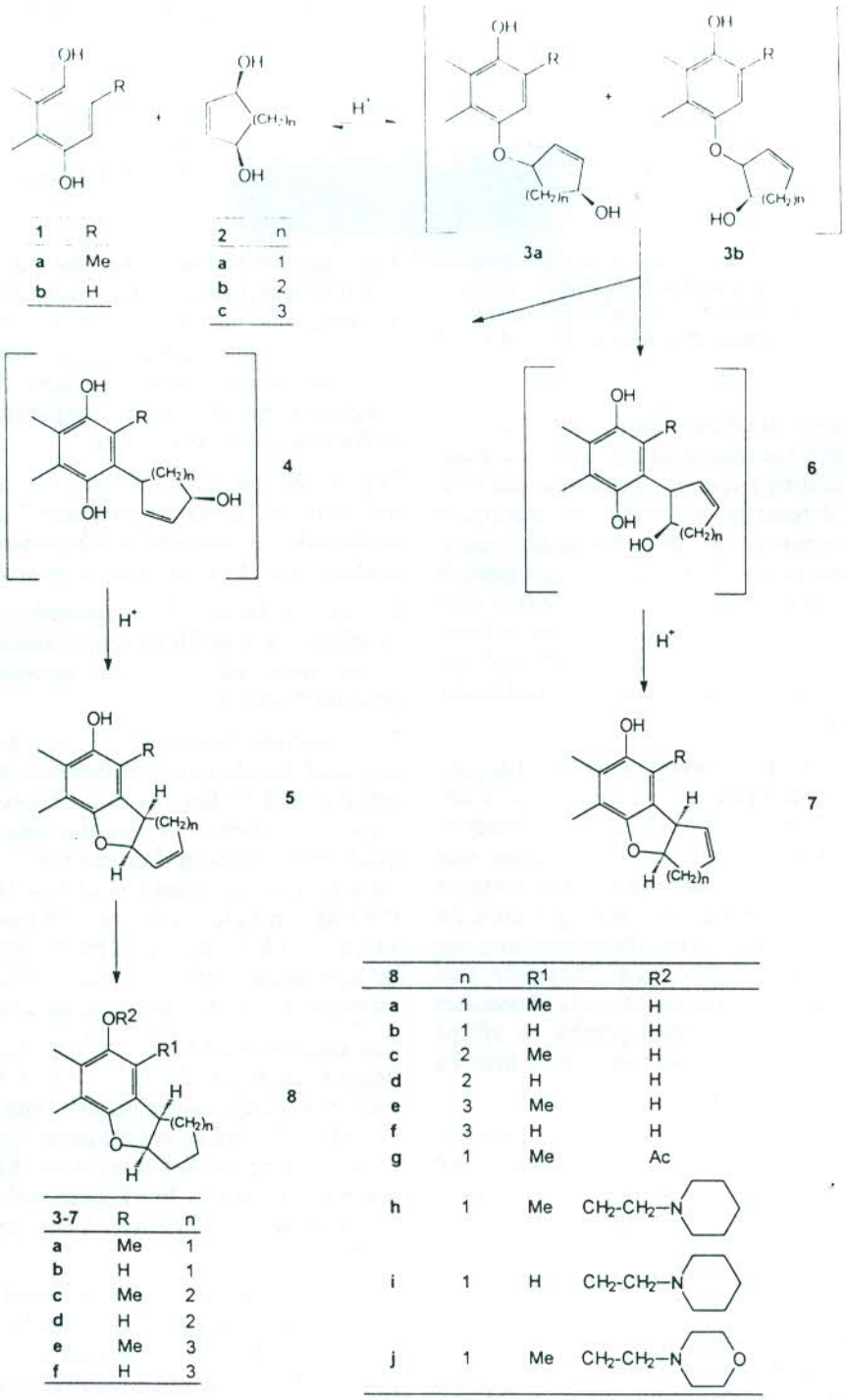
It may also be possible to postulate the initial formation of ethers **3a** and **3b** by simultaneous S_N2 and S_N2' processes, followed by 3,3-rearrangements to furnish compounds **5** and **7**.[12]

The reaction between 2,3-dimethylhydroquinone (**1b**) and diol **2a** also yielded benzofuranols **5b** and **7b** in a ratio of 4:1.[13] Besides these expected products, a pentacyclic compound **11** was also isolated as an inseparable mixture of *trans*- and *cis*-isomers, where the descriptors *cis* and *trans* are used to indicate the stereochemistry of the ring junctures to the central benzene ring (Scheme 3, **11a** and **11b**, ratio 3:2). The formation of the latter may be envisaged with two consecutive sequences of ether formation, 1,3-shift and cyclization via intermediate **5b**.

The generality and scope of the discussed reactions were demonstrated by the reactions of hydroquinone **1** with cyclohex-2-ene-1,4-diol (**2b**)[14] and cyclohept-2-ene-1,4-diol (**2c**).[15] In all cases, the reactions led to the formation of a mixture of benzofuranols **5c–f** and **7c–f**. Only the main products **5c–f** were isolated in pure state by repeated recrystallization of the crude isomeric mixture (Table 1).

The stereochemistry of compounds **5a–e** was assigned by X-ray structure analysis of the benzoate of **5b** (Figure), and by NOE experiments on compounds **5b–e**. Compound **5b** with two five-membered rings was expected to be *cis*-fused. The MM2 calculations indicated a considerably higher energy for the corresponding *trans*-fused diastereomer ($\Delta\Delta E$ = 12 kcal/mol). The X-ray structure determination of its benzoate derivative provided the proof of *cis*-stereochemistry (Figure).

For the six- and seven-membered ring compounds **5c–e**, the MM2 calculations showed approximately the same energy for the *cis*- and *trans*-fused isomers. However, nuclear Overhauser enhancement data showed similar interactions of the ring-juncture hydrogens for these compounds to those observed for **5b**. Considering the NOE data, the force-field calculations, and the similar mechanism of their formations we assumed *cis*-fused stereostructure for compounds **5a–e**.



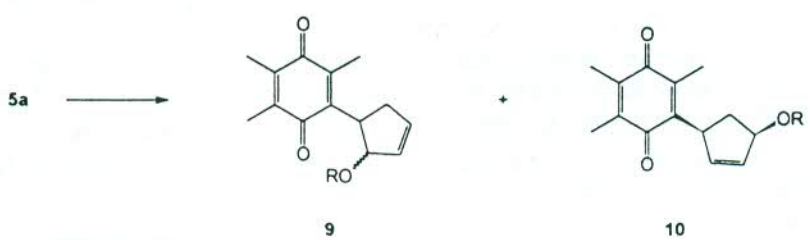
1	R
a	Me
b	H

2	n
a	1
b	2
c	3

3-7	R	n
a	Me	1
b	H	1
c	Me	2
d	H	2
e	Me	3
f	H	3

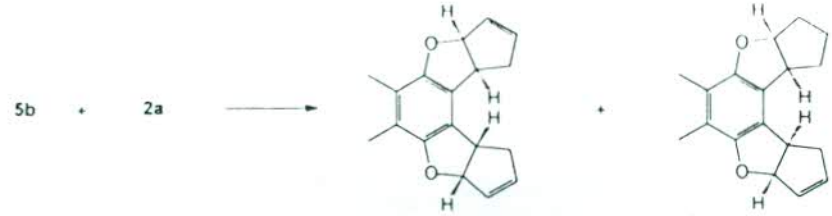
8	n	R^1	R^2
a	1	Me	H
b	1	H	H
c	2	Me	H
d	2	H	H
e	3	Me	H
f	3	H	H
g	1	Me	Ac
h	1	Me	CH_2-CH_2-N
i	1	H	CH_2-CH_2-N
j	1	Me	CH_2-CH_2-N O

Scheme 1



9,10	R
a	Me
b	Et
c	Pr

Scheme 2



Scheme 3

Table 1. Physical Properties of Benzofurans **5a–e**

Product	Starting Materials		Reaction Conditions		Yield (%)	mp (°C) (solvent)	TLC (R_f)	HPLC (t_R) (min)	Isomer Product		
			Temp. (°C)	Time (h)						Yield (%)	HPLC t_R (min)
5a	**1a**	**2a**	70	40	57	140 (EtOH)	0.3[a]	14.15[b]	**7a**	15	13.2
5b +	**1b**	**2a**	70	30	34	159 (EtOH)	0.42[a]	5.18[c]	**7b**	16	5.9
11a/b					6	216 (hexane)	0.55[a]	1.90/ 1.93[e]	–	–	–
5c	**1a**	**2b**	70	30	28	122 (hexane)	0.6[d]	–	**7c**	–	–
5d	**1b**	**2b**	70	3	26	140 (hexane)	0.7[d]	–	**7d**	–	–
5e	**1a**	**2c**	75	6	30	118 (hexane)	0.62[d]	9.2	**7e**	8	10.02
5f	**1b**	**2c**	75	6	35	122 (hexane)	0.68[d]	–	–	–	–

[a] Hexane/acetone (5 : 2).
[b] Hexane/CH_2Cl_2 (75 : 25).
[c] MeOH/H_2O (60 : 40).
[d] Hexane/Et_2O (1 : 1).
[e] i-Pr_2O/hexane/CH_2Cl_2 (10 : 45 : 45).

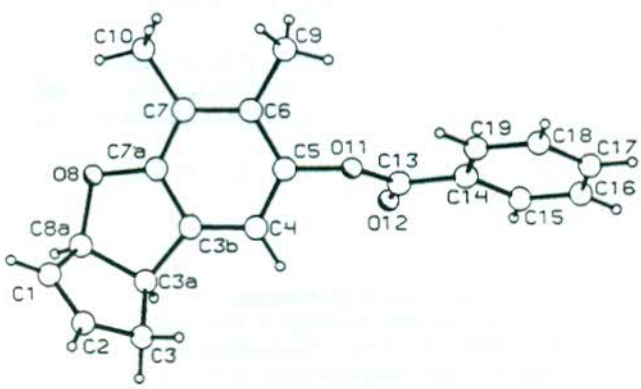


Figure. Crystal Structure of the Benzoate of **5b**.

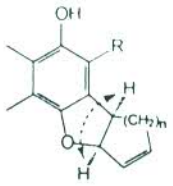
The partially saturated analogs **8b–f** were prepared by catalytic hydrogenation of the appropriate benzofuran **5**, in good yield. Then, new benzofuran derivatives **8g–j** were synthesized via standard acylation and alkylation processes from **8a–f** and the corresponding acylation and alkylation reagents (Table 2).

In conclusion, we have shown that the in situ generated allyl aryl ethers **3** show profound tendency for thermal 1,3-rearrangement and acid-catalyzed cyclization of the products **4** affords benzofuran derivatives **7**. This one-pot procedure for the preparation of benzofurans promises to have wide application in synthesis. All new compounds are of potential biological interest.

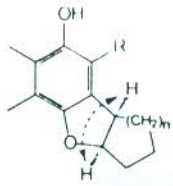
Table 2. Benzofuran Derivatives **8a–j** Prepared

Starting Material	Product	Reagent	Yield (%)	mp (°C)	TLC R_f	HPLC t_R (min)
5a	**8a**	H_2/Pd-C	86	141	0.50[a]	7.8[b]
5b	**8b**	H_2/Pd-C	63	142	0.55[a]	7.3[b]
5c	**8c**	H_2/Pd-C	85	121–122	0.50[a]	–
5d	**8d**	H_2/Pd-C	60	124–126	0.49[a]	–
5e	**8e**	H_2/Pd-C	60	112–114	0.48[a]	–
5f	**8f**	H_2/Pd-C	33	126–127	0.53[a]	–
8a	**8g**	Ac_2O	85		0.80[a]	14.0[c]
8a	**8h** · HCl	1-(2-chloroethyl)piperidine	53	201–203	0.83[d]	
8b	**8i** · HCl	1-(2-chloroethyl)piperidine	50	202–203	0.66[d]	
8a	**8j** · HCl	4-(2-chloroethyl)morpholine	47	175–176	0.66[d]	

[a] Hexane/acetone (5 : 2).
[b] MeOH/H_2O (60 : 40).
[c] MeCN/H_2O/H_3PO_4 (60 : 40 : 0.25).
[d] Toluene/hexane/EtOH (60 : 40 : 0.25) satd with NH_3.



5



8

Compound	Irradiate	Observe	N.O.E.
5a	C3aH	C8aH	3.2 %
	C8aH	C3aH	1.9 %
5c	C4aH	C9aH	8.0 %
	C9aH	C4aH	6.6 %
5d	C4aH	C9aH	3.8 %
	C9aH	C4aH	3.8 %
5e	C5aH	C10aH	8.5 %
	C10aH	C5aH	6.3 %
8a	C3aH	C8aH	3.2 %
	C8aH	C3aH	3.5 %
8d	C4aH	C9aH	6.7 %
	C9aH	C4aH	7.7 %

Reagents were obtained from commercial suppliers and were used without further purification. All reactions were conducted under an atmosphere of dry N_2 or Ar. Melting points were determined on a Büchi apparatus and are uncorrected. IR spectra were obtained with a Spectromom 2000 spectrophotometer. ^1H and ^{13}C NMR spectra measurements were carried out using a VXR 400 spectrometer. All signals are expressed as δ values downfield from TMS used as an internal standard. MS spectra were obtained on a KRATOS MS25RFA spectrometer. HPLC analyses were performed on a DuPont 830 instrument equipped with UV detector, stationary phase: Nucleosil C-18 (250 × 4 mm). Satisfactory microanalyses were obtained for all new compounds: C, H ± 0.3.

Benzofurans 5a–f; General Procedure:

To a stirred mixture of hydroquinone **1** (0.2 mol) and (1*S*)-(+)-10-camphorsulfonic acid (2.0 g) in anhyd toluene (250 mL) was added the appropriate diol **2** (0.22 mol), and the resulting suspension was stirred for the specified period of time at the temperature shown in Table 1. After cooling, the precipitated product was filtered and recrystallized three times from EtOH or hexane to afford pure **5**. The yields of **5a–f** and their spectral data are summarized in Tables 1 and 3.

Separation of Isomeric Benzofurans 5a and 7a:

A mixture of **1a** (35.0 g, 0.23 mol), **2a** (25.0 g, 0.25 mol) and (1*S*)-(+)-10-camphorsulfonic acid (2.0 g, 8.6 mmol) in anhyd toluene (400 mL) was stirred at 100 °C for 24 h under Ar. After cooling, the precipitate was collected by filtration and recrystallized from EtOH to yield a 3:1 mixture of isomers **5a** and **7a** (27.3 g, 55 %).

5a-Acetate:

To a stirred solution of the above mixture of isomers **5a** and **7a** (14.4 g, 0.067 mol) in anhyd pyridine (70 mL) was added Ac_2O (10.8 g, 10 mL, 0.11 mol) and the resulting mixture was stirred at r.t. for 12 h. The mixture was poured into ice/H_2O and acidified with coned HCl. The resulting suspension was filtered, the solids were washed with H_2O and then recrystallized three times from EtOH to afford pure **5a-acetate**; yield: 5.8 g (34 %); mp 92–93 °C; TLC (hexane/acetone, 5:2): R_f 0.75; HPLC (hexane/CH_2Cl_2, 3:1): t_R 9.97 min.

IR (KBr): ν = 1740 (CO), 1440, 1360, 1190, 1060 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.98 (3 H, s, CH_3), 2.04 (3 H, s, CH_3), 2.08 (3 H, s, CH_3), 2.31 (3 H, s, CH_3), 2.51 (1 H, m-d, J = 17 Hz, CH_2), 2.88 (1 H, m-dd, J = 17, 7 Hz, CH_2), 4.05 (1 H, m-dd, J = 7, 2 Hz, CH), 5.80 (1 H, d, J = 10 Hz, CHO), 5.90 (1 H, m, CH=), 6.0 (1 H, m, CH=).

^{13}C NMR ($CDCl_3$): δ = 12.14 (C-6-CH_3), 12.72 (C-7-CH_3), 12.93 (C-4-CH_3), 20.39 ($COCH_3$), 39.93 (C-3), 43.83 (C-3a), 92.26 (C-8a), 116.84 (C-7), 123.26 (C-3b), 127.21 (C-4), 128.41 (C-6), 129.76 (C-2), 135.32 (C-1), 141.72 (C-5), 154.68 (C-7a), 169.34 (CO).

7a-Acetate:

The mother liquor of the first recrystallization was concentrated in vacuo and the resulting mixture was separated by repeated column chromatography with hexane/acetone (5:0.1, v/v) as eluent to yield pure **7a-acetate** (0.7 g); mp 97 °C; TLC (hexane/acetone, 5:2): R_f 0.78; HPLC (hexane/CH_2Cl_2, 3:1): t_R 11.07 min.

IR (KBr): ν = 1735 (CO), 1445, 1380, 1360, 1195 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.98 (3 H, s, CH_3), 2.08 (6 H, s, $2CH_3$), 2.31 (3 H, s, CH_3), 2.79 (2 H, m, CH_2), 4.34 (1 H, d, J = 7.5 Hz, CH), 5.41 (1 H, m, CHO), 5.76 (2 H, m, CH=CH).

^{13}C NMR ($CDCl_3$): δ = 12.05 (C-7-CH_3), 12.67 (C-6-CH_3), 12.93 (C-4-CH_3), 20.36 ($COCH_3$), 40.78 (C-1), 54.20 (C-3a), 86.15 (C-8a), 116.22 (C-7), 122.83 (C-3b), 125.05 (C-4), 128.21 (C-6), 129.26 (C-3), 129.82 (C-2), 141.66 (C-5), 155.56 (C-7a), 169.19 (CO).

Compound **7a**:

To a stirred solution of NaOMe, prepared from Na (0.15 g) in anhyd MeOH (20 mL), was added **7a-acetate** (0.5 g), and the resulting mixture was stirred at r.t. for 10 h. The solvent was evaporated in vacuo, the residue was taken up in H_2O (5 mL) and acidified with 10 % HCl. The precipitated product was filtered and recrystallized from EtOH to afford **7a** (0.13 g, 36.3 %); mp 144 °C; TLC (hexane/acetone, 5:1): R_f 0.33; HPLC (hexane/CH_2Cl_2, 3:1): t_R 13.20.

IR (KBr): ν = 3380 (OH), 1460, 1410, 1380, 1360, 1260, 1230, 1080 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.10 (3 H, s, CH_3), 2.12 (3 H, s, CH_3), 2.18 (3 H, s, CH_3), 2.8 (2 H, m, CH_2), 4.16 (1 H, s, OH), 4.35 (1 H, d-m, J = 5 Hz, CH), 5.38 (1 H, t-m, J = 5 Hz, CH), 5.9 (1 H, m, CH=), 5.98 (1 H, m, CH=).

^{13}C NMR ($CDCl_3$): δ = 12.01 (C-7-CH_3), 12.24 (C-6-CH_3), 12.53 (C-4-CH_3), 40.77 (C-1), 54.25 (C-3a), 85.56 (C-8a), 116.00 (C-4), 116.81 (C-6), 121.80 (C-7), 125.00 (C-3b), 129.26 (C-2), 129.94 (C-3), 145.60 (C-5), 151.46 (C-7a).

MS: m/z = 216 (M^+, 100), 201 ($M^+ - CH_3$, 30), 189 (35), 175 (16), 128 (10).

X-ray Structure Determination of 5b-Benzoate:

Determination of the unit-cell parameters and collection of the symmetry independent reflections of **5b-Benzoate** were performed on an Enraf-Nonius CAD4 computer-controlled single-crystal diffractometer using graphite monochromated MoK_α radiation (0.71073 Å) and $\omega/2\theta$ scan mode at 293(2) K. The selected single crystal had the dimension of 0.50 × 0.50 × 0.17 mm. The unit cell dimensions of the monoclinic crystals [a = 7.996(1) Å; b = 18.603(1) Å; c = 10.925(1) Å] were calculated using 25 reflections observed in the θ-range from 18.96° to 20.88°.

$C_{20}H_{18}O_3$ **(5b-Benzoate)** (prepared from **5b** by standard procedure[7]) crystallizes in the space group $P2_1/c$, Z = 4. The calculated density is 1.277 Mg · m^{-3}. 6538 reflections were collected between 2.82 to 33.03 θ angles within the $0 \le h \le 12$, $-28 \le k \le 0$, $-16 \le l \le 16$ index ranges. 6020 intensity data were found independent (R_{int} = 0.0171). Data reduction was carried out by program XCAD4 (Harms, 1996), while the empirical absorption correction (ψ-scan method) by MolEN (Enraf-Nonius, 1990). The maximum and minimum transmissions were 0.992 and 0.927, respectively. The initial structure model was found by direct methods (program SHELXS86)[17] while the structure refinement was done by SHELXL93.[18] Anisotropic displacement parameters were refined for all of the non-hydrogen atoms. Hydrogen atoms were introduced in calculated positions and refined riding on the respective carbon atoms. Further details of the X-ray structure determination may be obtained elsewhere.[19]

Table 3. Spectral Data for Substituted Benzofurans **5** and **8**

Product	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ	MS m/z (%)
5a	3380, 3050, 1460, 1260, 1210, 1080	2.10 (3 H, s, CH_3), 2.12 (3 H, s, CH_3), 2.17 (3 H, s, CH_3), 2.52 (1 H, d-m, J = 17, 2, CH_2), 2.92 (1 H, d-m, J = 17, 2, CH_2), 4.08 (1 H, t, J = 8, CH), 4.16 (1 H, s, OH), 5.79 (1 H, dd, J = 7.4, 2, CH-O), 5.91 (1 H, d-m, J = 6, 2.5, CH=), 6.00 (1 H, d-m, J = 6, 2.5, CH=)	12.06 (C-6-CH_3), 12.31 (C-7-CH_3), 12.60 (C-4-CH_3), 39.96 (C-3), 43.59 (C-3a), 91.62 (C-3b), 116.13 (C-4), 117.07 (C-6), 122.05 (C-7), 126.85 (C-7b), 129.82 (C-2), 135.09 (C-1), 145.72 (C-5), 150.44 (C-7a)	216 (M^+, 100), 201 (M^+-CH_3, 30), 189 (35), 175 (16)
5a-PNB[a]	1745, 1520, 1540, 1350, 1280, 1220	2.03 (3 H, s, CH_3), 2.09 (3 H, s, CH_3), 2.12 (3 H, s, CH_3), 2.55 (1 H, d-m, CH_2), 2.94 (1 H, m, CH_2), 4.12 (1 H, t, J = 8, CH), 5.85 (1 H, d-m, J = 8, CH-O), 5.95 (1 H, m, CH=), 6.05 (1 H, m, CH=), 8.38 (4 H, m, H_{arom})		365 (M^+, 22), 215 (M^+-NO_2-PhCO, 100), 200 (7), 187 (12), 150 (14)
5b	3350, 1450, 1380, 1360, 1270, 1205	2.11 (6 H, s, 2 CH_3), 2.52 (1 H, m, CH_2), 2.88 (1 H, m, CH_2), 3.8 (1 H, s, OH), 4.02 (1 H, m-t, J = 7.5, CH), 5.76 (1 H, d-m, J = 7.5, CH-O), 5.84 (1 H, m, CH=), 5.98 (1 H, m, CH=), 6.48 (1 H, s, H_{arom})	11.85 (C-6-CH_3), 12.29 (C-7-CH_3), 40.28 (C-3), 44.23 (C-3a), 91.53 (C-3b), 108.84 (C-4), 118.94 (C-6), 123.03 (C-7), 127.45 (C-7b), 130.08 (C-2), 134.64 (C-1), 138.74 (C-5), 150.38 (C-7a)	–
5b-Benzoate	1740, 1450, 1260, 1250, 1200, 1205	2.05 (3 H, s, CH_3), 2.12 (3 H, s, CH_3), 2.58 (1 H, m, CH_2), 2.82 (1 H, m, CH_2), 4.02 (1 H, t-m, J = 7.5, CH), 5.80 (1 H, m, CH-O), 5.90 (1 H, m, CH=), 5.98 (1 H, m, CH=), 6.7 (1 H, s, H_{arom}), 7.42 (3 H, m, H_{arom}), 8.22 (2 H, m, H_{arom})	–	202 (M^+, 100), 187 (M^+-CH_3, 15), 175 (38), 159 (8), 128 (6)
5c	3450, 1620, 1460, 1260, 1220, 1210, 1060	1.31 (1 H, m, CH_2), 1.9–2.1 (3 H, m, CH_2), 2.12 (3 H, s, CH_3), 2.19 (3 H, s, CH_3), 2.20 (3 H, s, CH_3), 3.15 (1 H, m, CH), 4.40 (1 H, s, OH), 4.76 (1 H, m, CH), 6.13 (1 H, d-m, J = 10, CH=), 6.20 (1 H, d-m, J = 10, CH=)	12.20 (C-5-CH_3), 12.23 (C-7-CH_3), 12.26 (C-8-CH_3), 23.99 (C-3), 24.68 (C-4), 40.36 (C-4a), 77.43 (C-4b), 116.33 (C-5), 116.96 (C-7), 121.43 (C-8), 124.19 (C-2), 128.27 (C-8b), 133.50 (C-1), 145.74 (C-6), 150.72 (C-8a)	230 (M^+, 100), 215 (M^+-CH_3, 24), 189 (28), 176 (32), 165 (27), 115 (17)
5d	3380, 1610, 1450, 1255, 1220, 1200, 1060	1.58 (1 H, m, CH_2), 1.90 (1 H, m, CH_2), 1.9–2.2 (2 H, m, CH_2), 2.12 (3 H, s, CH_3), 2.14 (3 H, s, CH_3), 3.30 (1 H, dd-m, J = 8, 2, CH), 4.41 (1 H, s, OH), 4.91 (1 H, dd-m, J = 8, 2, CH-O), 5.98 (1 H, dd, J = 10, 2, CH=), 6.10 (1 H, J = 10, 2, CH=), 6.52 (1 H, s, H_{arom})	11.78 (C-7-CH_3), 12.35 (C-8-CH_3), 22.79 (C-4), 25.12 (C-3), 40.61 (C-4a), 77.97 (C-4b), 108.19 (C-5), 119.41 (C-7), 121.97 (C-8), 124.68 (C-2), 128.05 (C-8b), 133.14 (C-1), 147.39 (C-6), 151.50 (C-8a)	216 (M^+, 100), 201 (M^+-CH_3, 21), 188 (12), 175 (16), 162 (9), 151 (28), 128 (6), 115 (7)
5e	3460, 1450, 1300, 1240, 1210, 1060	1.5–1.9 (6 H, m, 3 CH_2), 2.02 (6 H, s, 2 CH_3), 2.08 (3 H, s, CH_3), 3.25 (1 H, m, CH), 4.18 (1 H, s, OH), 5.22 (1 H, m, CH-O), 5.4–6.2 (2 H, m, CH=CH), 1.5–1.8 (5 H, m, 3 CH_2), 1.9 (1 H, m, CH_2), 2.09 (3 H, s, CH_3), 2.12 (3 H, s, CH_3), 2.16 (3 H, s, CH_3), 3.76 (1 H, t-m, J = 7, CH), 4.15 (1 H, s, OH), 5.20 (1 H, t-m, J = 7, CH-O)	–	–
8a	3400, 1460, 1410, 1370, 1300, 1250	1.5–1.8 (5 H, m, 3 CH_2), 1.9 (1 H, m, CH_2), 2.09 (3 H, s, CH_3), 2.12 (3 H, s, CH_3), 2.16 (3 H, s, CH_3), 3.76 (1 H, t-m, J = 7, CH), 4.15 (1 H, s, OH), 5.20 (1 H, t-m, J = 7, CH-O)	–	218 (M^+, 100), 203 ($M^+-C_2H_5$, 16), 189 ($M^+-C_3H_7$, 76), 175 (28), 145 (14), 115 (12)
8a-Benzoate	–	1.55–1.98 (5 H, m, 3 CH_2), 2.03 (3 H, s, CH_3), 2.07 (3 H, s, CH_3), 2.10 (1 H, m, CH_2), 2.11 (3 H, s, CH_3), 3.79 (1 H, t-m, J = 7, CH), 5.26 (1 H, dd-m, J = 7, 2, CH-O), 7.52 (2 H, t-m, J = 8, 1.5, H_{arom}), 7.64 (1 H, t-m, J = 7.5, 1.5, H_{arom}), 8.24 (2 H, d-m, J = 8, 1.5, H_{arom})	–	322 (M^+, 64), 217 (M^+-PhCO, 86), 189 (11), 105 (100)
8b		1.50 (1 H, m, CH_2), 1.6–1.9 (4 H, m, 2 CH_2), 2.05 (1 H, m, CH_2), 3.77 (1 H, t-d, J = 7, 1, CH), 4.41 (1 H, s, OH), 5.20 (1 H, t-m, J = 6, CH-O), 6.46 (1 H, s, H_{arom})		204 (M^+, 100), 189 (M^+-CH_3, 31), 175 (46), 161 (8), 150 (8)

Table 3. (continued)

Product	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ	MS m/z (%)
8c	3500, 1520, 1480, 1430, 1410, 1390, 1310, 1290, 1240	1.09 (1 H, m, CH_2), 1.22 (1 H, m, CH_2), 1.45–1.8 (4 H, m, 2 CH_2), 1.92 (1 H, m, CH_2), 2.13 (3 H, s, CH_3), 2.14 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 2.28 (1 H, m, CH_2), 2.95 (1 H, dd, m, J = 11, 6, CH), 4.21 (1 H, s, OH), 4.46 (1 H, m, CH-O)	11.99 (C-5-CH_3), 12.31 (C-7-CH_3), 12.32 (C-8-CH_3), 20.55 (C-1), 23.09 (C-4), 27.71 (C-3), 28.79 (C-2), 40.55 (C-4a), 81.61 (C-4b), 116.51 (C-5), 120.89 (C-8), 131.06 (C-8b), 145.65 (C-6), 151.27 (C-8a)	232 (M^+, 100), 203 ($M^+-C_2H_5$, 6), 189 ($M^+-C_3H_7$, 43), 178 (10), 165 (7), 115 (5)
8d	3420, 1460, 1420, 1210, 1160, 1060	1.32 (1 H, m, CH_2), 1.48 (4 H, m, 2 CH_2), 1.80 (2 H, m, CH_2), 1.92 (1 H, m, CH_2), 2.13 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 3.12 (1 H, q-m, J = 6, CH), 4.35 (1 H, s, OH), 4.58 (1 H, m, CH-O), 6.48 (1 H, s, H_{arom})		218 (M^+, 100), 203 (M^+-CH_3, 7), 188 (9), 175 (32), 164 (28), 151 (14), 138 (6), 105 (6)
8e	3490, 1450, 1230, 1200, 1050	1.2–1.5 (3 H, m, CH_2), 1.6–2.0 (6 H, m, 3 CH_2), 2.11 (3 H, s, CH_3), 2.13 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 2.25 (1 H, m, CH_2), 3.33 (1 H, m, CH), 4.16 (1 H, s, OH), 4.78 (1 H, m, CH-O)	12.03 (C-8-CH_3), 12.19 (C-9-CH_3), 12.30 (C-6-CH_3), 23.49 (C-3), 29.39 (C-2 and C-4), 31.40 (C-5), 31.59 (C-1), 47.50 (C-5a), 85.85 (C-5b), 115.45 (C-8), 117.05 (C-6), 121.53 (C-9), 127.85 (C-9b), 145.65 (C-7), 151.06 (C-9a)	204 (M^+, 100), 189 (M^+-CH_3, 31), 175 (46), 161 (8), 150 (8)
8f	3410, 1450, 1210, 1080	1.35 (3 H, m, CH_2), 1.75 (5 H, m, 3 CH_2), 1.90 (1 H, m, CH_2), 2.08 (1 H, m, CH_2), 2.12 (6 H, s, 2 CH_3), 3.48 (1 H, m, CH), 4.15 (1 H, s, OH), 4.86 (1 H, m, CH), 6.42 (1 H, s, H_{arom})	246 (M^+, 100), 203 ($M^+-C_3H_7$, 9), 189 ($M^+-C_4H_9$, 48), 175 (11), 165 (22), 145 (7), 115 (6)	232 (M^+, 100), 189 ($M^+-C_3H_7$, 16), 175 ($M^+-C_4H_9$, 34), 151 (46), 115 (10)
8g	1730, 1460, 1410, 1370, 1220, 1200, 1060	1.5–1.95 (5 H, m, 3 CH_2), 1.99 (3 H, s, CH_3), 2.04 (3 H, s, CH_3), 2.08 (3 H, s, CH_3), 2.10 (1 H, m, CH_2), 2.32 (3 H, s, CH_3), 3.75 (1 H, t-d, J = 6, 2, CH), 5.24 (1 H, m, CH-O)	–	260 (M^+, 17), 218 ($M^+-CH_2=C=O$, 100), 203 (4), 189 (18), 164 (6)
8h · HCl	1600, 1460, 1410, 1390, 1320, 1220, 1160, 1100, 1070, 1010	1.47 (2 H, m, CH_2), 1.53 (1 H, m, CH_2), 1.78 (2 H, m, CH_2), 1.90 (4 H, m, 4″-CH_2 and 5″-CH_2), 2.05 (3 H, s, CH_3), 2.08 (1 H, m, CH), 2.13 (3 H, s, CH_3), 2.21 (3 H, s, CH_3), 2.35 (2 H, m, CH_2), 2.93 (2 H, m, 6″-CH_2), 3.40 (2 H, t, J = 5, CH_2), 3.73 (3 H, m, CH-2″-CH_2), 4.23 (2 H, m, CH_2O), 5.22 (1 H, t-m, J = 7, 1.5, CH-O), 12.46 (1 H, br s, NH^+)	12.14 (C-7-CH_3), 13.05 (C-4-CH_3 and C-6-CH_3), 22.00 (C-4″), 22.76 (C-3″ and C-5″), 23.78 (C-2), 33.38 (C-1), 46.51 (C-3a), 54.14 (C-2″ and C-6″), 57.27 (C-2′), 66.90 (C-1′), 88.69 (C-3b), 115.54 (C-6), 123.35 (C-4), 127.59 (C-7), 128.24 (C-7b), 148.80 (C-5), 155.21 (C-7a)	329 (M^+, 3), 217 (5), 189 (4), 112 (100), 98 (63)
8h	–	1.66 (12 H, m, 6 CH_2), 2.06 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 2.19 (3 H, s, CH_3), 2.52 (4 H, m, 2 CH_2), 2.75 (2 H, t, J = 6, CH_2N), 3.71 (1 H, m, CH), 3.80 (2 H, t, J = 6, OCH_2), 5.19 (1 H, m, CH-O)	12.14 (C-7-CH_3), 12.64 (C-4-CH_3 and C-6-CH_3), 23.93 (C-2), 24.48 (C-4″), 26.09 (C-3″ and C-5″), 33.40 (C-1), 35.39 (C-3), 46.71 (C-3a), 55.28 (C-2″ and C-6″), 59.03 (C-2′), 70.70 (C-1′), 88.60 (C-3b), 115.28 (C-6), 123.85 (C-4), 127.24 (C-7), 128.79 (C-7b), 149.71 (C-5), 154.65 (C-7a)	–
8i · HCl	1620, 1600, 1470, 1450, 1430, 1380, 1330, 1300, 1250, 1200, 1100, 1080	1.47 (2 H, m, CH_2), 1.53 (1 H, m, CH_2), 1.78 (2 H, m, CH_2), 1.90 (4 H, m, 4″-CH_2 and 5″-CH_2), 2.03 (1 H, m, CH_2), 2.07 (3 H, s, CH_3), 2.10 (3 H, s, CH_3), 2.28 (2 H, m, CH_2), 2.87 (2 H, m, 6″-CH_2), 3.41 (2 H, m, CH_2N), 3.67 (2 H, m, 2″-CH_2), 3.79 (1 H, t-m, J = 7, 1, CH), 4.45 (2 H, m, OCH_2), 5.21 (1 H, t-m, J = 7, 1, CH-O), 6.56 (1 H, s, H_{arom}), 12.40 (1 H, br s, NH^+)	–	315 (M^+, 4), 203 (3), 112 (100), 98 (92)
8i	–	1.2–1.8 (12 H, m, 6 CH_2), 2.05 (6 H, s, 2 CH_3), 2.48 (4 H, m, 2 NCH_2), 2.7 (2 H, t, J = 6, CH_2N), 3.75 (1 H, m, CH), 3.98 (2 H, t, J = 6, OCH_2), 5.06 (1 H, m, CH-O), 6.5 (1 H, s, H_{arom})	–	–

Table 3. (continued)

Product	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$, TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$, TMS) δ	MS m/z (%)
8j·HCl	1620, 1600, 1470, 1460, 1410, 1380, 1330, 1270, 1220, 1120, 1080, 1040	1.54 (1 H, m, CH_2), 1.6–1.8 (3 H, m, $2CH_2$), 1.8–2.0 (1 H, m, CH_2), 2.06 (3 H, s, CH_3), 2.08 (1 H, m, CH_2), 2.13 (3 H, s, CH_3), 2.21 (3 H, s, CH_3), 3.18 (2 H, br s, 6″-CH_2), 3.48 (2 H, m, CH_2O), 3.70 (1 H, br s, CH), 3.72 (2 H, t-m, 2″-CH_2), 4.02 (2 H, m, OCH_2), 4.27 (2 H, m, OCH_2), 4.35 (2 H, m–t, CH_2O), 5.22 (1 H, m, CH-O), 13.42 (1 H, br s, NH^+)	12.11 (C-7-CH_3), 13.08 (C-6-CH_3), 13.28 (C-4-CH_3), 23.84 (C-2), 33.43 (C-1), 35.31 (C-3), 46.57 (C-3a), 53.06 (C-2″ and C-6″), 57.77 (C-2′), 63.77 (C-3″ and C-5″), 66.90 (C-1′), 88.78 (C-3b), 115.66 (C-6), 123.35 (C-4), 127.71 (C-7), 128.27 (C-7b), 148.86 (C-5), 155.32 (C-7a)	331 (M^+, 3), 217 (4), 189 (3), 114 (100), 100 (26)
8j	1580, 1460, 1400, 1390, 1310, 1215, 1100, 1080	1.4–2.0 (6 H, m, $3CH_2$), 2.06 (3 H, s, CH_3), 2.14 (3 H, s, CH_3), 2.18 (3 H, s, CH_3), 2.59 (4 H, m, $2CH_2N$), 2.78 (2 H, t, J = 6, CH_2N), 3.6–3.9 (7 H, m, $3CH_2O$), 5.20 (1 H, m, CH-O)	12.17 (C-7-CH_3), 12.67 (C-4-CH_3 and C-6-CH_3), 23.93 (C-2), 33.40 (C-1), 35.36 (C-3), 46.69 (C-3a), 54.44 (C-2″ and C-6″), 58.80 (C-2′), 67.07 (C-3″ and C-5″), 70.32 (C-1′), 88.66 (C-3b), 115.40 (C-6), 123.79 (C-4), 127.33 (C-7), 128.76 (C-7b), 149.56 (C-5), 154.74 (C-7a)	
11	1600, 1450, 1400, 1380, 1250, 1080	2.05 (6 H, s, $2CH_3$), 2.6–3.0 (4 H, m, $2CH_2$), 4.0 (2 H, m, 2 CH), 5.8 (2 H, m, 2 CH-O), 5.98 (4 H, s, 2 CH=CH)	–	266 (100, M^+), 251 (38), 237 (21), 225 (16), 165 (7), 152 (5), 128 (6)

* PNB = *p*-Nitrobenzoate.

2-(2-Methoxycyclopent-3-enyl)-3,5,6-trimethyl-1,4-benzoquinone (9a) and 2-(4-Methoxycyclopent-2-enyl)-3,5,6-trimethyl-1,4-benzoquinone (10a):

To a stirred solution of **5a** (4.8 g, 22 mmol) in MeOH (150 mL) was added dropwise a solution of $FeCl_3 \cdot 6H_2O$ (68 g) in a mixture of MeOH (680 mL) and H_2O (150 mL) during 1 h and the resulting mixture was stirred at r.t. for 1.5 h. H_2O (340 mL) was added and the mixture was extracted several times with CH_2Cl_2 (400 mL). The combined organic extracts were washed with H_2O and dried ($MgSO_4$). Evaporation of the solvent gave a mixture of two compounds which was separated by column chromatography (hexane/acetone, 10:1) to afford **9a** and **10a**; yields: 1.5 g (28%) and 1.1 g (20%), respectively.

Compound **9a**:

Yellow oil; TLC (hexane/acetone, 5:1): R_f 0.4.

IR (film): ν = 1620, 1460, 1425, 1360, 1340, 1280, 1250, 1210, 1180, 1100, 1080 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.98 (3 H, s, CH_3), 2.04 (3 H, s, CH_3), 2.10 (3 H, s, CH_3), 2.65 (2 H, m, CH_2), 3.29 (3 H, s, OCH_3), 3.38 (1 H, m, CH), 4.62 (1 H, m, CH-O), 5.95 (2 H, m, CH=CH).

MS: m/z = 246 (M^+, 60), 231 ($M^+ - 15$, 28), 214 ($M^+ -$ MeOH, 27), 188 (24), 175 (20), 71 (100).

Compound **10a**:

Light yellow oil; TLC (hexane/acetone, 5:1): R_f 0.38.

IR (film): ν = 1625, 1450, 1360, 1280, 1250, 1210, 1190, 1100, 1080, 1000 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.98 (3 H, s, CH_3), 2.00 (1 H, m, CH_2), 2.02 (3 H, s, CH_3), 2.04 (3 H, s, CH_3), 2.21 (1 H, m-dd, J = 13, 2 Hz, CH_2), 3.35 (3 H, s, OCH_3), 4.36 (1 H, m-dd, J = 8, 2 Hz, CH), 4.69 (1 H, m-dd, J = 8, 2 Hz, CH-O), 5.97 (1 H, m-dd, J = 6, 2 Hz, CH=), 6.02 (1 H, m-dd, J = 6, 2 Hz, =CH).

^{13}C NMR ($CDCl_3$): δ = 11.76 (C-3-CH_3), 12.20 (C-5-CH_3 and C-6-CH_3), 36.42 (C-5′), 43.35 (C-1′), 55.96 (OCH_3), 86.26 (C-4′), 130.55 (C-2′), 138.27 (C-3′), 140.32 (C-6), 140.93 (C-5), 141.46 (C-3), 144.53 (C-2), 186.77 (C-1), 187.44 (C-4).

MS: m/z = 246 (M^+, 38), 214 ($M^+ -$ MeOH, 100), 199 (42).

Compound **9b**:

Yield (31%); yellow oil; TLC (hexane/EtOAc, 20:1): R_f 0.69.

IR (film): ν = 1630, 1450, 1380, 1360, 1280, 1000 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.15 (3 H, t, J = 6 Hz, CH_3), 2.3–2.7 (2 H, m, CH_2), 3.35 (1 H, m, CH), 3.40 (2 H, q, J = 6 Hz, CH_2O), 4.7 (1 H, m, CH-O), 5.9 (1 H, m, CH=), 6.00 (1 H, m, =CH).

Compound **10b**:

Yield (18%); yellow oil; TLC (hexane/EtOAc, 20:1): R_f 0.64.

IR (film): ν = 1630, 1450, 1380, 1360, 1280, 1100, 1080 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.22 (3 H, t, J = 6 Hz, CH_3), 1.98 (3 H, s, CH_3), 2.00 (1 H, m, CH_2), 2.02 (3 H, s, CH_3), 2.06 (3 H, s, CH_3), 2.2 (1 H, m-dd, J = 12, 2 Hz, CH_2), 3.52 (2 H, q, J = 6 Hz, CH_2O), 4.35 (1 H, m-dd, J = 8, 2 Hz, CH), 4.75 (1 H, m-dd, J = 8, 2 Hz, CH-O), 5.9 (1 H, m-dd, J = 6, 2 Hz, CH=), 5.98 (1 H, m-dd, J = 6, 2 Hz, =CH).

^{13}C NMR ($CDCl_3$): δ = 11.82 (C-3-CH_3), 12.21 (C-6-CH_3), 12.27 (C-5-CH_3), 15.53 (OCH_2CH_3), 36.45 (C-5′), 42.99 (C-1′), 64.07 (OCH_2), 84.49 (C-4′), 130.59 (C-2′), 138.08 (C-3′), 140.11 (C-6), 140.72 (C-5), 141.33 (C-3), 144.19 (C-2), 186.80 (C-1), 187.48 (C-4).

Compound **10c**:[16]

Yield (24%); light yellow oil; TLC (hexane/EtOAc, 20:1): R_f 0.67.

IR (film): ν = 1630, 1440, 1380, 1360, 1290, 1240, 1110, 1080 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.93 (3 H, t, J = 7 Hz, CH_3), 1.57 (2 H, m-q, J = 7 Hz, CH_2), 1.7–2.3 (2 H, m, CH_2), 1.99 (6 H, s, $2CH_3$), 2.03 (3 H, s, CH_3), 3.43 (2 H, t, J = 7 Hz, CH_2O), 4.36 (1 H, m-t, J = 8 Hz, CH), 4.75 (1 H, m, CH), 5.94 (2 H, m, CH=CH).

^{13}C NMR ($CDCl_3$): δ = 10.65 ($OCH_2CH_2CH_3$), 11.82 (C-3-CH_3), 12.23 (C-5-CH_3 and C-6-CH_3), 23.43 (OCH_2CH_2), 36.83 (C-5′), 43.32 (C-1′), 70.70 (OCH_2), 84.86 (C-4′), 131.13 (C-2′), 137.77 (C-3′), 140.32 (C-6), 140.96 (C-5), 141.46 (C-3), 144.68 (C-2), 186.89 (C-1), 187.59 (C-4).

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