*Revue Roumaine de Chimie*, **2008**, *53*(3), 195–202

# 1,2,3,3a,4,6a-HEXAHYDRO-1,3-PENTALENEDIMETHANOL, *MONO* AND *BIS* OH-PROTECTED DERIVATIVES, USEFUL INTERMEDIATES FOR FINE ORGANIC SYNTHESIS

Constantin I. TĂNASE,[a*] Florea G. COCU,[a] Constantin DRĂGHICI[b] and Miron T. CĂPROIU[b]

[a] National Institute for Chemical & Pharmaceutical Research and Development, 112 Vitan Av., 74373 Bucharest 3, ROUMANIA*
[b]Center for Organic Chemistry "C. D. Nenitzescu", 202B Splaiul Independentei, Bucharest 060023, ROUMANIA

*Received March 7, 2007*

A high yield synthesis of 1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol **4**, useful intermediate in synthesis of natural product analogues and in fine organic synthesis is described. This stable, crystallized compound was protected to one or both hydroxymethyl groups, resulting diprotected derivatives with acyl- (**5a-e, 7**), ether-(**8a-b**) and tert-butyldimethylsilyl ether (**8c**) and also the corresponding monoprotected derivatives **6a-h**. The new compounds were characterized by IR, $^{1}$H- and $^{13}$C-NMR spectra.

## INTRODUCTION

In the previous papers[1,2] we presented the synthesis of new carbacyclin type compounds, "*pseudo*-carbacyclins", starting from 2α,4α-dimethanol-bicyclo[3.3.0]octene-6, 1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol **4** or its *mono*protected derivatives **6** (Scheme 1-3).

Preliminary communications[3] about the synthesis of compound **4**, and some *mono*protected compounds **6** and *bis*-OH-protected compounds **5** were already done. In this paper we present a full description of their synthesis and the characterization of the new compounds by IR and NMR spectroscopy. The first high yield synthesis of 1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol **4** and of the *mono*- and *bis*-OH-protected compounds **6**, **7**, **8** and **5** with acyl, silyl and ether protective groups is fully described. 1,2,3,3a,4,6a-Hexahydro-1,3-pentalenedimethanol and its OH-protected derivatives are valuable intermediates for the synthesis of carbacyclin and prostaglandin analogues and other fine chemicals.

Previously, the bicyclo[3.3.0]oct-6-ene intermediate **4** was mentioned in the literature[4] as one of the products identified in the oxidative photoaddition of $Me_2N$-NO and $Me_2N$-$NO_2$ to *endo*-dicyclopentadiene (*endo*-DCPD), after reduction of the reaction mixture with $LiAlH_4$ in modest yield in a mixture with a plenty of other compounds.

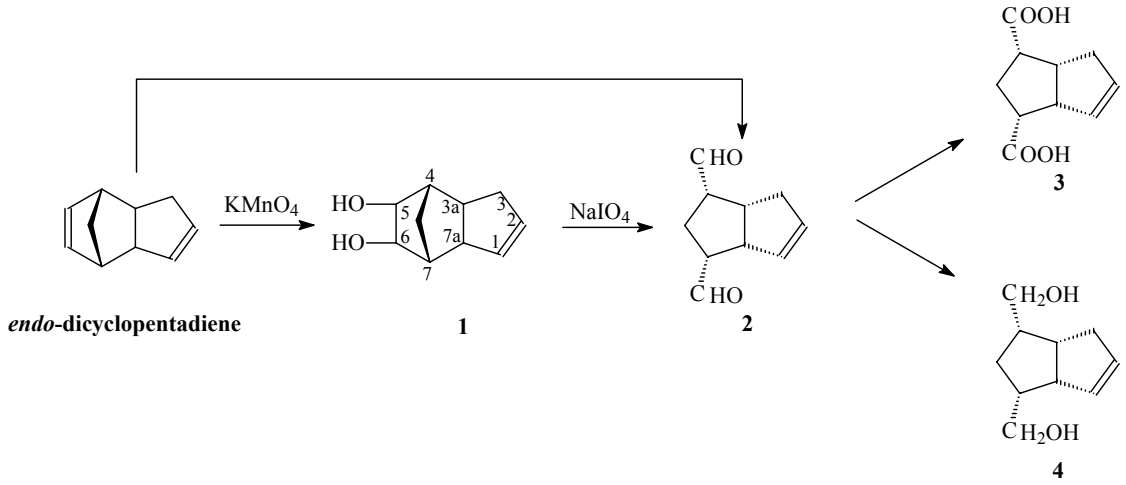
## RESULTS AND DISCUSSION

Our synthesis started from 5-*exo*,6-*exo*-dihydroxy-*endo*-3a,4,5,6,7,7a-hexahydro-4,7-methanoindene **1** (easily obtained from *endo*-dicyclopentadiene in 28%[5] to 83%[6] yield by permanganate hydroxylation) which was oxidatively cleaved with $NaIO_4$ in quantitative yield to the dialdehyde **2**, as mentioned in the literature[5]. This dialdehyde intermediate (**2**) was also obtained by direct hydroxylation of *endo*-DCPD in anhydrous dichloromethane with $KMnO_4$ in the presence of an equivalent of the phase transfer agent (triethylbenzylammonium chloride) TEBA to the corresponding cyclic hypomanganate ester, and then acid hydrolysis (81% yield[6], the procedure was not reproduced in our laboratory) or by ozonolysis of *endo*-DCPD, in cyclohexane-methanol at reduced temperature (in these conditions the resulted ozonide being insoluble and protected to further degradation), followed by decomposition of the ozonide with dimethylsulfide to the dialdehyde **2** in quantitative yield[7] (the conditions are hazardous to be used on a multimolar scale synthesis).

* Corresponding author: cvtanase@gmail.com

In all the synthesis presented, the aldehyde group was used in Grignard reaction[5] or oxidized to carboxyl, obtaining the diacid intermediate **3**[7] (Scheme 1).

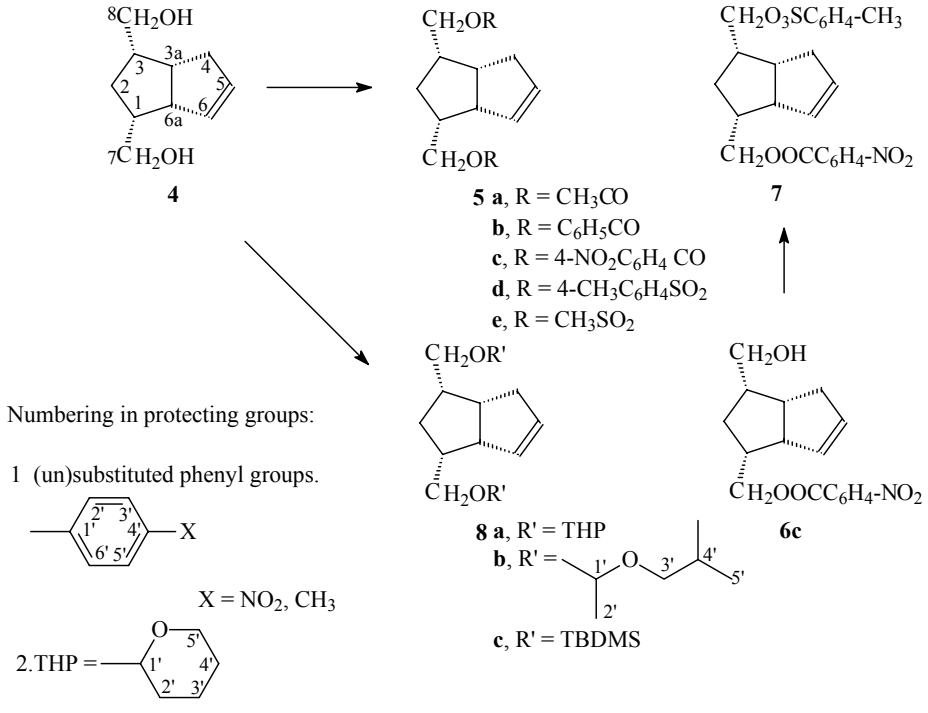
We reduced the dialdehyde groups with $NaBH_4$ to the primary alcohol groups obtaining in over 84% yield the stable, crystallized compound **4**.




Scheme 1 – Synthesis of 1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol **4**.

The molecular structure of the compound make it very attractive for synthesis of a variety of intermediates or products using the functional groups existing in the molecule: the exocyclic hydroxymethyl groups, *endo* on the bicyclo[3.3.0] octenic skeleton and endocyclic double bond, in the requested following chemical reactions.

The proper steric configuration of the hydroxymethyl group, more closely to the double bond (C-6 of the double bond), make it to interfere in the normal way of the reactions on the double bond, (in many reactions even regioselectively and in high yield[8]), reducing the expected yield. So, for majority of the reactions on the double bond, both exocyclic hydroxymethyl groups must be protected with adequate protecting groups, as in compounds **5** (Scheme 2).




Scheme 2 – Synthesis of disubstituted derivatives of 1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol **4**.

When the synthetic strategy require that only one of the hydroxymethyl groups to be used in next steps, as is the case for synthesis of *pseudo*carbacyclins[1,2], then it is necessary to realize a monoprotection of one hydroxymethyl group, as in compounds **6** (Scheme 3).

### Protection of both hydroxymethyl groups

During our synthetic works we found it useful to protect the hydroxymethyl groups as:

1. ester, these groups being stable in acid and neutral conditions, some groups even in slightly basic conditions. For our studies we need to use protective groups that introduce from the *endo* side of the molecule and implicitly of the double bond an increase steric hindrance: acetate < mesylate< benzoate < *p*-toluenesulphonate ≤ *p*-nitrobenzoate ≈a mixed *p*-toluenesulphonate and *p*-nitrobenzoate.

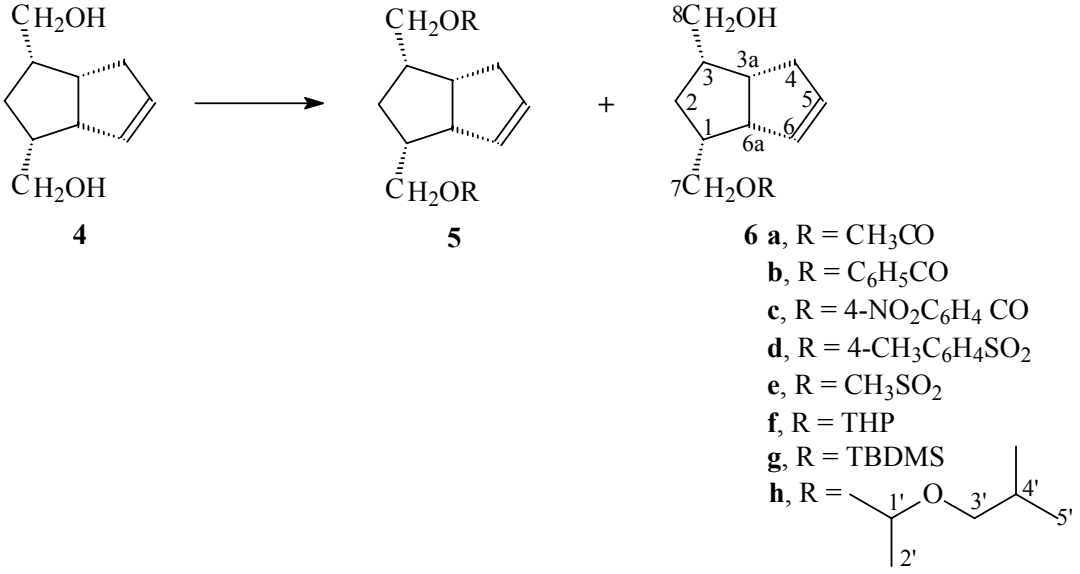
2. ether or silylether, groups stable in basic and neutral conditions. For protecting the hydroxymethyl group we use 3,4-dihydro-2H-pyran, isobutylvinylether, *tert*-butyldimethyl-chlorosilane.

Diesters were synthesized by usual procedures, obtaining in high yields pure crystallized compounds: diacetate, dimesylate, ditosylate, di-*p*-nitrobenzoate, a mixed ester *p*-toluenesulphonate and *p*-nitrobenzoate, easy purified by simple crystallization. Only dibenzoate was obtained as oil and purified by pressure chromatography, but it is pure enough for further use in reactions.

Diethers were also obtained in almost quantitative yields as oils, enough pure to be use in next reactions. For analytic characterization these diethers were purified by pressure chromatography, obtaining viscous, uncolored oils.

### Protection of one hydroxymethyl group

For protecting only one of the hydroxymethyl groups, the specified reaction was carried out using a 1:1 molar ratio between the reagents or a slight excess of the acylating or etherifying reagent.




**6** **a**, R = $CH_3CO$
**b**, R = $C_6H_5CO$
**c**, R = 4-$NO_2C_6H_4$ CO
**d**, R = 4-$CH_3C_6H_4SO_2$
**e**, R = $CH_3SO_2$
**f**, R = THP
**g**, R = TBDMS
**h**, R = 


Scheme 3 – Synthesis of monosubstitued derivatives of 1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol **4**.

*Table 1*

Monoprotection of the intermediate **4**

| R | Reagent/**4** | **4** (%) | **5** (%) | **6** (%) |
|---|---|---|---|---|
| acetyl | 1:1 | 21.6 | 24.6 | 50.4 |
| benzoyl | 1:1 | 29.1 | 26.6 | 50.4 |
| *p*-nitrobenzoyl | 1.15:1 | 39.6 | 32.2 | 27.2 |
| methansulfonyl | 1.05:1 | undetermined | ~24 | ~50 |
| | 1.7:1 | 21.0 | 47.13 | 24.8 |
| tetrahydropyranyl | 1.19:1 | 14.9 | 32.04 | ~49 |
| *t*-butyldimethylsilyl | 1.49:1 | ~28 | ~50 | ~22 |
| | 1.85:1 | not recovered | 45 | 39.8 |
| Isobutoxy-ethoxy | 1.2:1 | not recovered | 31.7 | 40.6 |

In these conditions, the desired monoprotected compound **6** was obtained in the yield presented in Table 1, together with the corresponding diprotected derivative **5** and unreacted diol **4**. Separation of this reaction mixture was easily made by pressure chromatography, the $R_f$ difference of the compounds allowing their isolation in almost quantitative yield (of the products formed in the reaction). When we need to obtain in high yield both mono and *bis*-OH-protected compounds, we use an excess of acylating or etherifying reagent, 1.3 to 1.6 equivalents or more.

So, we obtained in high yield the hexahydropentalenedimethanol intermediate **4**, the diprotected derivatives with acyl- (**5a-e**), ether- (**8a-b**) and *tert*-butyldimethylsilylether (**8c**)-protecting groups and the corresponding monoprotected derivatives **6a-h**, key intermediates for selective functionalization at the double bond or at the free hydroxymethyl group. The use of compounds **2**, **4** and some monoprotected derivatives **6** in synthesis of new analogues of carbacyclin with unconventional positions of the side chains, "*pseudo*carbacyclins", was already presented.[1, 2] The use of intermediate **4** and bis-protected derivatives **5** and **8** in functionalization of the double bond will be presented in separate papers.

## EXPERIMENTAL

Melting points were determined in open capillary and are uncorrected. Progress of the reaction was monitored by TLC on Merck silica gel 60 or $60F_{254}$ plates (Merck) eluted with the solvent system: (I). benzene: ethyl acetate: hexane (5:3:2), (II). ethyl acetate: hexane: acetic acid (5:4:0.1) (v: v: v). IR spectra were recorded on Specord 75 IR spectrometer. $^1$H-NMR and $^{13}$C-NMR spectra are recorded on Varian Gemini 300 BB spectrometer (300 MHz for $^1$H and 75 MHz for $^{13}$C, respectively), chemical shifts are given in ppm relative to TMS as internal standard. The numbering of the compounds is presented in Schemes 1-3.

### Structural aspects

The compounds were analyzed by elemental analysis, IR, $^1$H- and $^{13}$C-NMR spectra, or only some of them, and also MS for the compound **4**, confirming their structure.

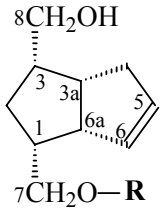
Compound **4** has characteristic in IR spectrum two bands for the double bond (3040, 1615 $cm^{-1}$), a broad band (3400-3270 $cm^{-1}$) and two medium bands (1070 and 1010 $cm^{-1}$) for the hydroxyl groups, which appear also in monoprotected compounds; in the *bis*-protected derivatives the hydroxyl bands are not present. *Mono*- and *bis*-protected compounds presents in IR spectra the characteristic bands for protecting groups.

The double bond in **4** creates a disymmetry of the molecule observable in $^1$ H- and $^{13}$C-NMR spectrum. The methylene protons of hydroxymethyl groups appear at different chemical shifts: 3.40, 3.38(dd, H-8) and 3.32, 3.28(dd, H-7) as a result of their diastereotopicity. At different chemical shifts appear also the protons from the bicyclic skeleton. In $^{13}$C-NMR all carbon atoms appear at different δ values. The same profile is observed for all *bis*-protected derivatives ($^1$H- and $^{13}$C-NMR spectra are presented at the experimental part). Other spectra were recorded in mono or bi dimensional-NMR sequencies [APT, COSY(H-H), COSY(C-H), NOE, decoupling and TFA addition, variable temperature] in order to make correct attribution of the signals.

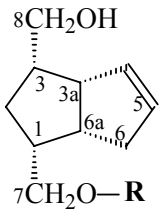
By derivatization of the hydroxylic groups to mono protected compounds, always results two isomers **A** and **B**, which are non separable by TLC methods. This complicates the proton spectra and also, in $^{13}$C-NMR spectra the carbon atoms appear as two set of signals (See experimental part). Two sets of signals in $^{13}$C-NMR spectra accounts for mixture of isomers are presented in the literature[10].

For the tetrahydropyranyl derivative **6f** another 2 isomers, C and D, appear, because of the α or β acetalic bond to C-1' of THP protecting group. This makes olefinic carbon atoms to appear in NMR spectrum for example as four signals at δ= 132.44, 132.28, 131.88, 131.82 for C-5 and 3 signals for C-6 at δ= 130.15, 130.06, and 129.69. (This profile is observed similarly for **8a**).

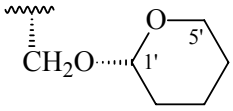
Analytical data confirmed the proposed structure of the compounds.



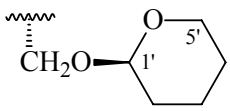

**A**




**B**




**C**




**D**

### 1. Synthesis of 1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol 4

*1.1. Synthesis of 5,6-dihydroxydicyclopentadiene* **1**

The starting compound, 5,6-dihydroxydicyclopentadiene [(±)-5-exo,6exo-dihydroxy-*endo*-3α,4,5,6,7,7α,-hexahydro-4,7-methanoinden] was synthesized by an improved procedure[5,8] from *endo*-dicyclopentadiene by $KMnO_4$ hydroxylation in basic (KOH) aqueous-alcohol solution in the presence of TEBA-Cl as phase transfer catalyst[8]; the crude viscous oil (crystallizes in time) was recrystallised from benzene-ligroin, resulting a white product, m.p. 58-59ºC (lit.[5] 48-51ºC), $R_f$= 0.14, characterized by elemental analysis: calcd. For $C_{10}H_{14}O_2$: Th. C: 72.26%, H: 8.48%; found: C: 71.80%,

H: 8.49%, IR(KBr, $cm^{-1}$): 3600-3200, and 3030 $cm^{-1}$ and $^1$H-NMR (60MHz, $CDCl_3$, $\delta$ ppm, *J* Hz ) : **5.88**(s, 2H, H-2-3); **3.87**(d, 1H, $J_{5,6}$=6.5, H-6 or H-5); **3.78**(d, 1H, $J_{5,6}$=6.5, H-5 or H-6); **3.10**(s, 2H, HO-$C_5$, HO-$C_6$; with TFA-$d_1$ moved to 6,90); **1.98-3.09**(m,6H, H-1,3a,4,7,7a); **1.86**(d, 1H, $J_{gem}$=11.0, H-8); **1.31**(d, 1H, $J_{gem}$=11.0, H-8).

*1.2. 1α,3α-Diformyl-1,2,3,3a,4,6a,- hexahydropentalene* **2**

To a cooled (-10ºC) solution of 164.6g(0.754 moles) 98% $NaIO_4$ in 1.4 L water, in inert ($N_2$)atmosphere was added slowly a solution of 120 g (0.722 moles) dihydroxydicyclopentadiene **1** in 500 mL ethanol, maintaining the reaction mixture under -2ºC. Another 250 mL ethanol were added to dissolve the dialdehyde formed, the stirring was continued for 1 hr, monitoring the reaction by TLC (I, $Rf_1$= 0.14, $R_{f2}$~0.52). The resulted $NaIO_3$ was filtered, washed with 400 mL ethanol, the filtrate concentrated under reduced pressure and the aqueous solution extracted with ethyl ether (4x0.3L). By concentrating the dried ether extracts (anh. $Na_2SO_4$), dialdehyde **2** resulted in quantitative yield. An aliquote of dialdehyde was crystallized from ethyl ether-hexane, the product having m.p. 44-45ºC and characteristic signals in IR(KBr, $cm^{-1}$): 3060, 2810, 1720 $cm^{-1}$. The $^1$H-NMR($CCl_4$, δ ppm, *J* Hz) spectra recorded at 60 MHz shows the very specific signals of aldehyde: **9.73**(d, 1.0), **9.63**(d, 2.0) and double bond: **5.60**(m, 2H) groups.

*1.3. (±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydro-1,3-pentalenedimethanol* **4**

To a solution of 60 g (0.36 moles) 2α,4α-diformylbicyclo [3.3.0]oct-6-ene **2** in 1L methanol, cooled to -10ºC, was added a solution of 30.6 g(0.792 moles) 98% $NaBH_4$ in 0.5L water, for 30 min., maintaining the reaction under 0ºC . The mixture was stirred 1 h (TLC monitoring, I, $Rf_2$=0.52, $Rf_4$~0.08.), 70 mL acetic acid slowly added, methanol distilled under reduced pressure, the aqueous solution extracted with ethyl acetate (4x250 mL), organic extracts washed with sat. $NaHCO_3$ soln. (2x150 mL), brine (2x150 mL), dried over anh. $MgSO_4$, filtered off and evaporated. The crude product was crystallized from ethyl acetate, resulting 47 g (84% yield) of pure title compound, **4,** m.p. 86,5-87,5ºC (twice recrystallized). From the mother liquors 7 g of a slightly impure product were also obtained.

The product was analyzed by: elemental analysis, $C_{10}H_{16}O_2$ Calc. (%): C: 71.39, H: 9.59 found. (%): C:71.35; H:9.50, IR(KBr, $cm^{-1}$): 3400-3270, 3040, 2920-2900, 2870, 1615, 1440, 1405, 1360, 1070, 1010, 730, $^1$H-NMR(dmso-$d_6$, δ ppm, *J* Hz)**: 5.67** (dq, 1H, H-5, 5.8, 2.2); **5.57**(dq, 1H, H-6, 5.8, 2.2); **4.36**(t, 1H, HO-, deuterable, 5.0); **4.33** (t,1H, HO-, deuterable; 5.0)**; 3.40**(ddd,1H.H-8, 9.9; 6.8, 5.0); **3.38**(ddd,1H,H-8, 9.9, 6.8, 5.0); **3.32** (ddd,1H,H-7, 10.4, 8.0, 5.0); **3.28**(ddd,1H,H-7, 10.4, 4.5, 2.2); **3.15**(m,1H,H-6a; 8.0, 8.5 (coupling with H-3a or/and H-1), 4.5, 2.2 (couplings with H-6 and H-5)); **2.75** ($q_v$,1H, H-3a, 8.0); **2.19**(ddd, 2H, H-4, 2.2, 4.5, 8.0); **2.10-1.96**(m, 2H, H-1-3); **1.57**(dt,1H, syst. AB, H-2A, 12.3, 5.5); **0.59**(q, 1H, syst. AB, H-2B, 12,3), $^{13}$C-NMR(dmso-d6, δ ppm): **131.49**(C-5); **132.35**(C-6 ); **62.55** (C-7); **62.15**(C-8); **51.58**(CH,C-6a); **45.91**(C-1 or C-3); **45.22**(C-3 or C-1); **41.42**(C-3a); **32.82**(C-4); **31.09**(C-2). Mass spectrum, [$M^+$] : 168 (MP).

## 2. Synthesis of diacylated compounds 5a-e

2.1. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydropentalene-1α,3α-dimethanol-diacetate* **5a**

10g(59.4 mmoles) Diol **4**, dissolved in 45 mL pyridine was acetylated in usual conditions (0ºC 2 hrs, then at r. t. over night) with 14.3 mL (0.148 moles) acetic anhydride, monitoring the reaction by TLC (I, $Rf_1$~0.08, $Rf_{2a}$~0.75). The reaction mixture was poured on crashed ice and extracted with dicloromethane (2x100 mL); the unified organic extracts were washed with: 2N HCl (2x100 mL), satd. $NaHCO_3$ soln. (100 mL), brine (100 mL) and dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The crude product, 14.7 g, was crystallized from ligroin (b.p. 81-85ºC), resulting 14.2 g (94.7%) pure compound (**5a**), m.p. 32-34ºC, characterized by: elemental analysis, $C_{14}H_{20}O_4$ Calc. (%):C: 66.64, H: 7.99, found. (%):C: 66.50; $^1$H-NMR-300MHz ( $CDCl_3$,δ ppm, J Hz): **5.75**(dq, 1H, H-5, 2.2, 5.8); **5.52**(dq, 1H, H-6, 2.2, 5.8); **4.10**(d, 2H, H-7, 7.5); **4.02** (d, 2H, H-8, 7.5); **3.30**(dt, H-6a, 8.5, 2.2); **2.90**(dq, H-3a, 8.5, 5.2); **2.38-2.26**(m, 3H, H-1-3.H-4A); **2.19**(ddq, syst. AB, 1H, H-4B, 2.2, 6.9, 17.5); **2.06**(s, 6H, CH$_3$); **1,74**(dt, 1H, syst. AB, H-2A, 5.5,12.4); **0.91**(dt, syst. AB, 1H, H-2B$_\alpha$, 12.4; 5.5). $^{13}$C-NMR ($CDCl_3$,δ ppm): **171.03**(COO); **132.62**(C-5); **129.16**(C-6); **65.88**(C-7); **65.60**(C-7); **51.78**(C-6a); **42.17**(C-1 or C-3); **42.07**(C-3 or C-1); **41.58**(C-3a); **33.28**(C-4); **31.27**(C-2); **20.91**($CH_3$).

2.2. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydropentalene-1α,3α-dimethanol-dibenzoate* **5b**

Diol **4**, 10 g(59.4 mmoles) was dissolved in 45 mL pyridine was esterified, as in 2.1., with 18.6 mL(22.5 g; 160 mmoles) 99% benzoylchloride, monitoring the reaction by TLC (I, $Rf_{2b}$~0,83). The crude product, 24 g, sufficient pure for use in many reactions, was purified by pressure chromatography (eluent: dichlorometane), resulting 22.1 g (98.8%) pure uncoloured or slight yellow oil, with: IR($CHCl_3$, $cm^{-1}$): 3050, 2890, 2050, 1705, 1600, 1580, 1450, 1260-1210, 1150, and 955. $^1$H-NMR($CDCl_3$, δ ppm, *J* Hz): **8.05**(dt, 4H, 1.5, 7.4)**; 7.55**(tt, 2H, 7.4, 1.5); **7.43**(dt, 4H, 1.5, 7.4); **5.79**(dq, 1H, H-5, 2.2, 5.7); **5.63**(1H, H-6, 2.3, 5,7); **4.42**(dd, 1H, H-7, 7.1, 11.1); **4.35**(dd, 1H, H-7, 8.1, 11.1); **4.33**(dd, 1H, H-8, 7.1, 10.9); **4.27**(dd, 1H, H-8, 8.2, 10.9); **3.42**(t, H-6a, 8.5); **3.02**(dq, H-3a, 5.6, 8.5); **2.59-2.43**(m, 2H, 2H-4); **2.39-2.27**(m, 2H, H-1-3); **1.88**(dt, 1H, syst. AB, H-2A, 5.4, 12.4); **1.10**(q, syst. AB, 1H, H-2B$_\alpha$, 12.4), $^{13}$C-NMR($CDCl_3$, $\delta$ ppm): **166.38** (COO); **132.78**(C-4'); **132.67**(C-5); **130.27**(C-1'); **129.43**(C-2'); **129.26**(C-6); **128.25**(C-3'); **66.21**(C-7); **65.94**(C-8); **51.91**(C-6a); **42.35**(C-1 or C-3); **42.20**(C-3 or C-1); **41.72**(C-3a); **33.38**(C-4); **31.16**(C-2).

2.3. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahidro-1,3-pentalenodimethanol-bis-p-nitrobenzoate* **5c**

20.2g(0.12 moles) 20.2g(0.12 moles) Diol **4** in 140 mL pyridine was esterified with 66.6 g (57.9 g 100%, 0.312 moles) *p*-nitrobenzoylchloride (87% purity), added in portions during 3 hrs at 0ºC. Stirring was continued for 2 hrs on ice-water bath and 3 days at room temperature (TLC, I, $R_{f5c}$ ~0.86). The reaction mixture was poured on crashed ice, the precipitate filtered, washed with water, air dried, resulting 64.5 g crude product. This was dissolved in ethylacetate (300mL), solution was washed with 2x200 mL sat. $NaHCO_3$ soln., 200 mL brine, dried over $Na_2SO_4$, filtered and concentrated until begins to crystallize, cooled and filtered off. The filtrate was concentrated similarly and a second crop was obtained; resulted 46.7 g(83.5%) pure *bis*(*p*-nitrobenzoate) **5c**, m.p. 139-141ºC, characterized by: elemental analysis: $C_{24}H_{22}N_2O_8$: calc. (%): C:61.79, H: 4.75, N: 6.01, found (%): C:61.70, H: 4.78, N:5.82. IR(KBr, $cm^{-1}$): 3050, 2925, 2890, 1705, 1590, 1510, 1330, 1460, 1250, 1090, 860, 830. $^1$H-NMR($CDCl_3$, δ ppm, *J* Hz): **8.31**(d, 4H, H-3', 8.5); **8.21**(d, 4H, H-2', 8.5); **5.84** (dd,1H, H-5, 5.6, 2.0); **5.63**(sext,1H, H-6, 5.6, 2.3); **4.49**(dd, syst AB,1H, H-7A, 11.0, 7.2); **4.42**(m, 1H, syst. AB, H-7B);

**4.45-4.37**(m, 2H, H-8); **3.46**(t, 1H, H-6a, 8.0); **3.06**(m, 1H, H-3a); **2.62-2.48**(m, 2H, H-4); **2.45-2.36**(m 2H, H-1-3); **1.91**(dt, 1H, syst. AB, H-2A, 12.3, 5.3); **1.14**(q,1H, syst. AB, H-2B, 12.3), $^{13}$C-NMR($CDCl_3$, δ ppm): **164.57**(COO); **150.49**(C-4'); **135.59, 135.56**(C-1'-1"); **133.04** (C-6); **130.64**(C-2'); **128.29**(C-5); **123.55**(C-3'); **67.17**(C-7 or C-8); **66.91**(C-8 or C-7); **51.93**(C-6a); **42.29**(C-1 or C-3); **42.23** (C-3 or C-1); **41.66**( C-3a); **33.46**(C-4); **31.21**(C-2).

### 2.4. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahidro-1,3-pentalenedimethanol-bis(4- toluene-sulfonate)* **5d**

Diol **4**, 2.53 g (15 mmoles) was esterified similarly with 8.58 g (45 mmoles) 4-toluene sulfonylchloride in 40 mL pyridine (TLC monitoring, I, $R_{f5d}$~0.83). The reaction mixture was poured under stirring on ice, the crystallized compound filtered, washed with water and air dried. It was obtained 7.04 g crude product which was recrystallised from ethyl acetate, resulting 6.04 g (84.5% yield), m.p. 104-106ºC, characterized by: elemental analysis, $C_{24}H_{28}S_2O_6$: calc. (%): C: 60.48, H: 5.92, S:13.45, found (%): C:60.89, H: 5.87, S:13.10. IR(KBr, $cm^{-1}$): 3030, 2910-2880, 2840, 1585, 1440, 1350, 1170, 950, 800-780, 660, and 550. $^1$H-NMR($CDCl_3$, *δ* ppm, *J* Hz):**7.77**(d, 4H, H-*o*; 8.2); **7.35**(d, 4H, H-*m*; 8,2); **5.65**(dq,1H, H-5, 5.7, 2.2); **5.35**(dq,1H, H-6, 5.7, 2.3); **4.01**(AB syst., 1H; H-7, $J_{AX}$ =7.1; $J_{BX}$=8.1; $J_{AB}$=9.7);**; 3.98**(AB syst., 1H; H-7, $J_{AX}$ =7.1; $J_{BX}$=8.1; $J_{AB}$=9.7); **3.92**(AB syst., 1H; H-8; $J_{AX}$ =9.0; $J_{BX}$=7.2; $J_{AB}$=9.5);**; 3.90**(AB syst., 1H; H-8; $J_{AX}$ =9.0; $J_{BX}$=7.2; $J_{AB}$=9.5); **3.24**(dt, 1H, H-6a, 8.2, 1.5); **2.85** (dq, 1H, H-3a; 5.0, 8.2 ); **2.45** (s, 6H, $CH_3$); **2.36-2.16** (m 3H, H-1-3-4); **1.97** (m, 1H, H-4); **1.63** (dt, 1H, syst. AB, H-2A, 12.4, 5.5); **0.74**(q,1H, syst. AB, H-2B, 12.4). $^{13}$C-NMR($CDCl_3$, *δ* ppm): **144.81**(C-1'); **133.11** (C-5); **129.84**(C-2'); **128.45**(C-6); **127.81**(C-3'); **71.43**(C-7); **71.17** (C-8); **51.47**(C-6a); **42.22**C-1 or C-3)**; 41.78** (C-3 or C-1); **41.63**(C-3a); **33.07**(C-4); **30.83**(C-2); **21.63** ($CH_3$).

### 2.5. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahidro-1,3-pentalenodimethanol- bis-methane-sulfonate,* **5e**

14g(0.083 moles) Diol **4** dissolved in 50 mL pyridine, was mesilated as in 2.4. with 22 mL (32.4 g, 0.283 moles) methanesulfonyl chloride (TLC, I, $R_{f5e}$~0.40; II, $R_{f5e}$~0.60). The reaction mixture was poured on ice, extracted with ethyl acetate (3x300 mL), unified organic extracts washed with satd. $NaHCO_3$ soln. (2x150 mL), brine (150 mL), dried ($MgSO_4$), concentrated, coevaporated with toluene and crystallized from ethyl acetate-hexane. Resulted 24.5 g (91%), crystallized compound **5e**, m.p. 73-74ºC, characterized by: elemental analysis, $C_{10}H_{20}S_2O_6$: calc. (%): C:38.76, H:6.85, S:21.78, found (%): C:38.64, H:6.71, S: 21.53; $^1$H-NMR($CDCl_3$, δ ppm *J* Hz): **5.81**(dq, 1H, H-5, 2.2, 5.7); **5.56**(dq, 1H, H-6, 2.3, 5.7); **4.26**(d, 2H, H-7, 7.6); **4.20**(dd, 1H, H-8, 8.1, 9.6); **4.14**(dd, 1H, H-8, 7.3, 9.6); **3.38**(dt, 1H, H-6a, 8.7, 2.3); **3.02**(s, 6H, $CH_3$)**; 2.97**(m, 1H, H-3a); **2.47**(dt, 1H, H-1 or H-3, 5.3, 7.3, 8.1); **2.43**(m, 1H, H-3 or H-1); **2.37**(ddt , 1H, H-4, 1.9, 2.2, 9.7); **2.20**(m, 1H, H-4) **1.85**(dt, 1H, syst. AB, H-2A, 5.3, 12.4); **0.97**(q, 1H, syst. AB, H-2B, 12.4). $^{13}$C- NMR ($CDCl_3$, δ ppm): **133.29**(C-5); **128.39**(C-6); **70.87**(C-7); **70.62**(C-8)**; 51.52**(C-6a); **42.44**(C-3); **41.85**(C-1-3a); **37.26**($CH_3$); **33.15**(C-4); **30.59**(C-2).

### 2.6. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahidro-1,3-pentalenodimethanol p-nitrobenzoate 4-toleunesulfonate 7*

6.6 g (20.8 mmoles) Mono *p*-nitrobenzoate **6c** were tosylated as above (see 2.4.) with 5.26 g (27 mmoles) 4-toluene sulfonylchloride (TLC, I, $R_{f7}$~0.77). The crude crystallized product (10.4 g) was recrystallised from ethyl acetate-hexane, resulting 7.91 g (81.3%) pure compound **7**, m.p. 108.5-110ºC, characterized by: elemental analysis, $C_{24}H_{25}NSO_7$: calc. (%): H:5.35, S:6.80, found (%):H:5.28, S:6.75; IR(KBr, $cm^{-1}$): 3040, 2880, 2840, 1710-1690, 1590, 1520, 1450, 1350, 1270, 1170, 1095, 940 and 810; $^1$H-NMR ( $CDCl_3$,δ ppm, *J* Hz): **8.29**(d, 2H, H-3', 9.0 *nitro*); **8.19**(d, 2H, H-2', 9.0 *nitro*); **7.80**(d, 2H, H-2', 8.3, *tosyl*); **7.36**(d, 2H, H-3', 8.3, *tosyl*); **5.74**(dq,1H, H-5, 2.2, 8.0); **5.55**(dq, 0,5H, H-6, 2.3, 5.8); **5.42**(dq, 0,5H, H-6, 2.3, 5.8); **4.38**(dd, 1H; H-7, 3.0, 7.7); **4.30**(d, 1H; H-7, 7.7); **4.07-3.97**(m, 2H, H-8) **3.35**(m, 1H, H-6a, 8.3); **2.96**(m, 1H, H-3a, 8.3); **2.46**(s, 3H, $C\underline{H}_3$); **2.53-2.03**(m, 4H, H-1-3, 2H-4); **1.80**(dt, 1H, syst. AB, H-2Aβ, 12.3, 5.4); **0.94**(dq, 1H, syst. AB, H-2Bα, 12.3, 2.9). $^{13}$C-NMR ($CDCl_3$, δppm): **164.48** ($\underline{C}$OO); **150.47**($C_q$-4'); **144.75**(C-1', in Ts); **135.55; 135.52**(C-1', in nitro); **133.13; 133.92**(C-5); **130.60**(C-2', in nitro); **129.81**(C-2', in Ts); **128.81; 128.59**(C-6); **127.81**(C-3', in Ts); **123.50**(C-3'); **71.60; 71.34**(C-8); **67.03; 66.77**(C-7,); **51.81; 51.52**(C-6a); **42.41;42.15**(C-1 or C-3); **42.09**( C-3 or C-1); **41.80; 41.48**(C-3a); **33.34; 33.12**(C-4); **31.59**(C-2); **21.59**($\underline{C}H_3$).

From mother liquors resulted also 1.04 g, slightly impure **7**.

## 3. Synthesis of diether compounds 8a-c

### 3.1. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahidro-1,3-pentalenodimethanol-bis(tetrahydropyran(2-yl)oxy* **8a**

To a solution of 16.82 g(0.10 moles) diol **4** and 50 mg TsOH in 180 mL $CHCl_3$, 20.2 mL(18.51 g; 0.22 moles) 3,4-dihydro-2H-pyran were added under stirring in 20 min., then stirred over night (TLC, II, $R_{f8a}$~0,86). The reaction mixture was washed with sat. $NaHCO_3$ sol. (50 mL), water (2x50 mL), brine (50 mL), dried ($MgSO_4$), concentrated. Resulted 33.2 g (98.6%) compound **8a** as oil, characterized by: $^1$H-NMR($CDCl_3$, *δ* ppm, *J* Hz): **5.71**(m, 1H, H-5); **5.63**(m, 0,5H, H-6); **5.23**(m, 0,5H, H-6); **4.60÷4.56**(m, 2H, H-1'); **3.87**(m, 2H, H-7-8); **3.81÷3.75**(m, 2H, H-5', 8.1); **3.66**(ddd, 1H, H-5', 2.6, 7.3, 9.5); **3.54÷3.48**(m, 2H, H-7-8); **3.39**(m,1H, H-5', 6.3); **3.28**(m, 1H, H-6a); **2.90**(m, 1H, H-3a); **2.34÷2.22**(m, 4H, H-1-3, 2H-4); **1.83-1.68**(3m, 4H, 2H-2', 2H-4'); **1.72**(dq, 1H, syst. AB, H-2A, 3.2, 12.4*)*; **1.63-1.47**(m, 8H, 2H-2', 4H-3', 2H-4'); **0.85**(q, 1H, syst. AB, H-2B, 12.4), $^{13}$C-NMR($CDCl_3$, *δ* ppm): **132.04; 131.98**(C-5); **130.13; 130.05**(C-6); **99.04; 99.00**($C\text{-}1'_7$); **98.99**($C\text{-}1'_8$); **69.45**(C-5'); **69.21; 69.18**(C-5'); **62.45**( C-7); **62.20; 62.18**(C-8); **51.99**(CH, C-6a); **43.36**(C-1); **42.75**(C-3); **42.20; 42.18**(C-3a); **33.42**(C-4); **31.91; 31.90**(C-2); **30.77**(C-4'); **25.47**(C-3'); **19.63**(C-2'); **19.48**(C-2').

### 3.2. *(±)-(1α,3α,3aβ,6aβ 1,3-Bis-(1-isobutoxy-ethoxymethyl)-1,2,3,3a,4,6a-hexahydro-pentalene* **8b**

10 g (59.4 mmoles) Diol **4**, were protected with 28 mL *iso*-butylvinylether in the conditions presented at 3.1. (2 g pyridinium tosylate were used instead of TsOH), resulting 32 g compound **8b** as slightly yellow oil (Tlc, I, $R_{f8b}$=0.89) characterized by: $^1$H-NMR($CDCl_3$, *δ* ppm, *J* Hz): **5.70**(m, 1H, H-5); **5.55**(m, 1H, H-6); **4.68-4.63**(m, 2H, H-1'); **3.63-3.41**(m, 4H, H-7-8); **3.40-3.28**(m, 2H, H-3'); **3.21-3.18**(m, 2H, H-3'); **3.27**(m, 1H, H-6a); **2.89**(m, 1H, H-3a); **2.26-2.08**(m, 4H, H-1-3, 2H-4); **1.88-1.78**(m, 2H, 2H-4'); **1.73**(m, 1H, syst. AB, H-2A); **1.30**(d, 6H, H-2', 5.4); **0.92**(d, 12H, H-5', 6.6); **0.81**(q, 1H, syst. AB, H-2B, 11.7), $^{13}$C-NMR($CDCl_3$, *δ* ppm): **132.02; 131.96**(C-5); **130.12; 130.07**(C-6); **100.08; 99.98**($C\text{-}1'_7$); **99.90; 99.82**($C\text{-}1'_8$); **72.54; 72.26; 77.07**(C-3'); **67.46**; **66.56**; **66.27**( C-7-8); **52.02**(C-6a); **43.46**(C-1); **42.84**(C-3); **42.14; 42.10**(C-3a); **33.37**(C-4); **31.85**(C-2); **28.65**($CH_3$-4'); **19.84; 19.77**(C-2'); **19.67; 19.50**(C-5').

3.3. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahidro-1,3-pentalenodimethanol- bis(tert-butyldimethyl silyloxy)* **8c**

10 g (59.4 mmoles) Diol **4** and 8.2 g (120 mmoles) imidazole were added in 110 mL $CHCl_3$, cooled to 0-5ºC and then, under stirring a solution of 23.5 g (155 mmoles) *tert*-butyldimethylsilyl chloride in 50 mL $CHCl_3$ was added dropwise. The reaction mixture was stirred over night (TLC, I, $R_{f8c}$~0,94), filtered, washed on filter with $CHCl_3$ and the solution was washed with satd. $NaHCO_3$ soln. (50 mL), water (2x50 mL), brine (50 mL), dried ($MgSO_4$), concentrated. Resulted 25 g of almost pure compound **8c** as colorless oil which was purified by pressure chromatography (eluent system I), giving 21.5 (91.2%) characterized by: $^1$H-NMR ($CDCl_3$, $\delta$ ppm, *J* Hz): **5.69**(dq, 1H, H-5, 2.3, 5.8); **5.58**(dq, 1H, H-6, 2.3, 5.8); **3.62**(d, 2H, H-7, 7.4); **3.55**(dd, 1H, H-8, 8.0, 9.8); **3.49**(dd, 1H, H-8, 7.0, 9.8); **3.28**(dt, 1H, H-6a, 8.5, 2.1); **2.85**(m, 1H, H-3a; 5.7, 8.5); **2.28-2.12**(m, 4H, H-1-3, 2H-4); **1.63**(dt, 1H, syst. AB, H-2A, 5.6, 12.4); **0.88**(s, 18H, $CH_3$); **0.73**(q, 1H, syst. AB, H-2B, 12.4); **0.04**(s, 12H, $CH_3$), $^{13}$C-NMR ($CDCl_3$, $\delta$ ppm): **131.74**(C-5); **130.33**(C-6); **64.78**(C-7 or C-8); **64.35**(C-8 or C-7); **51.87**(C-6a); **46.19**(C-1 or 3); **45.45**(C-3 or 1); **41.95**(C-3a); **33.28**(C-4); **30.93**(C-2), **25.92** ($\underline{C}H_3)_3C$; **18.26** $(CH_3)_3\underline{C}$; **5.33, 5.27**($\underline{C}H_3Si$).

## 4. Synthesis of monoacylated and monoether compounds 6a-h

4.1. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydropentalene-1α,3α-dimethanol-mono-acetate* **6a**

5.05 g (30mmoles) Diol **4** were acetylated with 2.9 mL (3.15 g; 30 mmoles) 97% acetic anhydride as in 2.1. (TLC, I, $R_{f6a}$ = 0.40; $R_{f5a}$ = 0.80). The crude reaction mixture, 5.9 g, containing monoacetate **6a**, diacetate **5a** and unreacted diol **4** was purified by pressure chromatography (system I), resulting: 1.68 g (24.6%) **5a**, 3.18 g (50.4%) **6a** and 1.09 g (21.6%) **4**. **6a**: oil, characterized by: elemental analysis, $C_{12}H_{18}O_3$: calc. (%):C:68.54, H:8.63, found (%):C:68.39, (%):H:8.54.

4.2. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydropentalene-1α,3α-dimethanol-mono-benzoate* **6b**

40.4 g (0.24 moles) Diol **4** were benzoylated with 28 mL (33.9 g; 0.241 moles) 99% benzoyl chloride as in 2.2. (TLC, I, $R_{f6b}$ = 0.38; $R_{f5b}$ = 0.83). The crude reaction mixture, 65 g, containing monobenzoate **6b**, dibenzoate **5b** and unreacted diol **4** was purified by pressure chromatography (system I or dichlorethane), resulting: 24 g (26.6%) **5b**, 29 g (44.1%) **6b** and 8 g (29.1%) **4**. **6b**: oil, IR($CHCl_3$, $cm^{-1}$): 3450-3350, 3040, 2910-2875, 1710, 1600, 1580, 1280-1230, 1115. $^1$H-NMR($CDCl_3$, $\delta$ ppm, *J* Hz): **8.04**(dd, 2H, H-*o*; 1.4, 7.4); 7**.56**(tt, 1H, H-*p*; 7.4, 1.4); **7.44**(tt, 2H, H-*m* 7.4, 1.4); **5.77**(m, 1H, H-5, 5.7, 2.2); **5.62**(m, 1H, H-6, 2.2, 5.7); **4.40**(dd, 0,5H, H-7, 7.3, 11.0); **4.36**(dd, 0,5H, H-7, 7.3, 11.0); **4.30**(dd, 0,5H, H-7, 8.0, 10.8); **4.25**(dd, 0,5H, H-7, 8.0, 10.8); **3.71**(d,1H, H-8, 8.0); **3.66**(dd, 0,5H, H-8, 7.5, 10.4); **3.60**(dd, 0,5H, H-8, 6.7, 10.4); **3.37**(m,1H, H-6a, 8.4); **2.97**(m,1H, H-3a, 5.3, 8.4); **2.43**(m, 1H, H-1); **2.36-2.23**(m, 4H, 2H-4, H-3, O$\underline{H}$); **1,81**(dt, 1H, syst. AB, H-2A, 5.5, 12.1); **0.97**(q, 1H, syst. AB, H-2B, 12.1), $^{13}$C-NMR($CDCl_3$, $\delta$ ppm): **166.60**(C=O); **132.88**(C-4'); **132.80; 132.34**(C-5); **130.48**(C-1'); **129,76, 129.43**(C-6); **129.57**(C-2'); **128.37**(C-3'); **66,52; 66.26**(C-7); **64.35; 64.13**(C-8); **52.14; 51.91**(C-6a); **46.11; 45.51**(C-3); **42.45, 41.89**(C-1-3a); **33.46; 33.18**(C-4); **31.14**(C-2).

4.3. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydropentalene-1α,3α-dimethanol-mono-4-nitro-benzoate* **6c**

20.2 g (0.12 moles) Diol **4** were 4-nitrobenzoylated with 26.5g (0.138 moles) 87% 4-nitrobenzoyl chloride as in 2.3. (TLC, I, $R_{f6c}$ = 0.36; $R_{f5c}$ = 0.86). The crude reaction mixture, 49 g, containing *mono* 4-nitrobenzoate **6c**, di-(4-nitrobenzoate) **5c** and unreacted diol **4** was purified by pressure chromatography (dichlorethane), resulting: 18.04 g (32.2%) **5c**, 8.63 g (27.2%) **6c** and 8.0 g (39.6%) **4**. **6c**: m.p. 104-105°C, elemental analysis: $C_{17}H_{19}NO_5$, (%):C: 64.34, H: 6.03, N:4.41, found: (%):C: 64.78, H: 5.70, N:4.10, IR (KBr, $cm^{-1}$): 3300-3175, 3020,2900, 2880, 2850, 1720, 1590, 1520, 1450, 1340, 1280, 1110, 1000, 940, 850, 935. $^1$H-NMR($CDCl_3$, $\delta$ ppm, *J* Hz): **8.32**(d, 2H, H-3', 8.7); 7**.23**(d, 2H, H-2', 8.7); **5.83**(dq, 0.5H, H-5, 5.7, 2.2); **5.80**(dq, 0.5H, H-5, 5.7, 2.2); **5.66**(dq, 0.5H, H-6, 5.7, 2.3); **5.66**(dq, 0.5H, H-6, 5.7, 2.3); **4.48**(dd, 0,5H, H-7, 7.4, 11.0); **4.42**(dd, 0,5H, H-7, 7.4, 11.0); **4.37**(dd, 1H, H-7, 7.7, 11.0); **3.75**(d, 1H, H-8, 7.4); **3.70**(dd, 0.5H, H-8, 7.4, 10.4); **3.64**(dd, 0,5H, H-8, 7.7, 10.4); **3.41**(m,1H, H-6a); **3.02**(m,1H, H-3a); **2.60-2.24**(m, 4H, H-1-3, 2H-4); **1,86**(dt, 1H, syst. AB, H-2A, 5.4, 11.7); **0.97**(q, 1H, syst. AB, H-2B, 11.7), $^{13}$C-NMR($CDCl_3$, $\delta$ ppm): **164.61**(C=O); **150.48**(C-4'); **135.70**(C-1'); **133.15, 132.19**(C-5); **130.63**(C-2'); **129,75, 128.98**(C-6); **123.52**(C-3'); **67,45, 67.20**(C-7); **64.24, 64.03**(C-8); **51.96, 51.84**(C-6a); **45.98, 45.50**(C-3); **42.25**(C-1); **41.91, 41.58**(C-3a); **33.39, 33.11**(C-4); **31.06**(C-2).

4.5.*(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydropentalene-1α,3α-dimethanol-mono-methane-sulfonate* **6e**

48.2g (0.2865 moles) Diol **4** were mesylated with 40 mL (58.96 g; 0.489 moles) ~95% methanesulfonyl chloride (It was used a greater molar ratio of 1.7:1) as in 2.5. At the molar ratio 1.05:1, the products determined by TLC were: ~24% **5e** and ~50% **6e**. After column chromatography purification, results 47.81 g (47.13%) **5e**, 17.44g (24.8%) **6e** and 10.1 g (21%) **4**. The methanesulfonate **6e** m.p. 77-78ºC; $^1$H-NMR($CDCl_3$, δ ppm, *J* Hz*):* **5.70**(dq, 1H, H-5; 2,2; 5,8); **5.59**(dq, 1H, H-6; 2,2; 5,8); **4.24**(dd, 1H, syst. AB, H-7A, 7.3, 9.9 ); **4.20**(dd, 1H, syst. AB, H-7B, 8.1, 9.9); **3.31**(dd, 1H, syst. AB, H-8A; 8.0, 10.4); **3.29**(dd, 1H, syst. AB, H-8B, 7.0, 10.4); **3.22** (dt, 1H, H-6a, 2.2, 8.3); **3.17**(s, 3H, $CH_3$); **2.80**(dt, 1H, H-3a, 6.0; 8.3); **2.31**(m, 1H, H-1, 5.3, 7.3, 8.1); **2.25-2.19**(m, 2H, H-4); **1.64**(dt, 1H, syst. AB, H-2A, 5.3, 12.4); **0.74**(q, 1H, syst. AB, H-2B; 12.4), $^{13}$C-NMR ($CDCl_3$): **131.31**(C-5); **130.20**(C-6); **71.65**(C-8); **62.28**(C-7); **51.61**(C-6a); **45.71**(C-3); **41.56**(C-1); **41.26**(C-3a); **36.42**($CH_3$); **32.81**(C-4); **30.58**(C-2).

4.6. *(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahydropentalene-1α,3α-dimethanol-mono-tetrahydropyran-(2-yl)oxy* **6f**

35.65 g (0.2119 moles) Diol **4** in 400 mL $CHCl_3$ were reacted with 23 mL (21.6 g, 0.25 moles) 3,4-dihydro-2H-pyran in the presence of 100 mg TsOH as described in 3.1 (TLC, II, $R_{f\ 6f}$= 0.63; $R_{f\ 5f}$= 0.86). After column purification (dichlorethane), results 22,87g(32,04%) **5f**, 24,28 g (45.21%) **6f**, as oil (also 2.25 g, 4%, impure **6f**) and 5.5 g **4**. For ester **6f** : $^1$H-NMR($CDCl_3$, $\delta$ ppm, *J* Hz): **5.73**(m, 1H, H-5, 2.1, 8.0); **5.62**(dq, 0,5H, H-6, 2.6, 8.5); **5.53**(dq, 0,5H, H-6; 2.6; 8.5) **4.59**(m, 1H, H-1', 2.7, 7.3); **3.86**(m, 1H, H-7); **3.77**(m, 1H, H-7); **3.68**(dd, 1H, H-8, 7.4, 9.5); **3.62**(dd, ~0,5H, H-5'; 7.3, 9.6); **3.58**(ddd, ~0,5H, H-5', 1.9, 6.7, 9.6); **3.51**(m, 1H, H-8); **3.41**(dd, 0,5H, H-5', 7.4, 9.6); **3.39**(dd, 0,5H, H-5', 7.0, 9.6); **3.34**(dd, 0,5H, H-6a, 7.7, 9.3); **3.29**(dd, 0,5H, H-6a, 7.2, 9.3); **2.91**(m, 1H, H-3a); **2.20÷2.14**(m, 4H, H-1-3, 2H-4); **1.81÷1.72**(m, 4H, H-2-2'-4', O$\underline{H}$); **1.58÷1.52**(m, 4H, 2H-3', H-2'-4'); **0.86**(dq, 1H, H-2, 12.2,), $^{13}$C-NMR($CDCl_3$, $\delta$ ppm): **132.44**; **132.38**; **131.88**; **131.82**(C-5); **130.15**; **130.06**; **129.69**(C-6); **99.18**; **98.93**(C-1'); **69.37; 6.35**(C-5'); **64.32; 64.30**(C-8); **62.34; 62.31**(C-7); **51.93; 51.91**(C-6a); **45.73; 45.72**(C-3); **43.03; 43.01**(C-1); **42.08; 42.06**(C-3a); **33.21; 33.19**(C-4); **31.31; 31.29**(C-2); **30.74**(C-4'); **25.45**(C-3'); **19.57; 19.55**(C-2')

4.7.*(±)-(1α,3α,3aβ,6aβ)-1,2,3,3a,4,6a-hexahidro-1,3-pentalenodimethanol-mono-tertbutyldimethylsilyloxy* **6g**

27.6(0.164 moles) Diol **4** in 75 mL pyridine was treated with 41 g (0.245 moles) ~90% *t*-butyldimethylsilyl chloride (the product ratio, determined qualitative by TLC, were: ~ 28% **4**, ~22% **8c** and ~50% **6g**) (TLC, I, $R_{f\ 6g}$= 0.69; $R_{f\ 8c}$= 0.94). The reaction was then continued adding another 20g reagent. After column chromatography purification, results 18.45 g (39.8%) **6g** as oil and 29.3g (45%) **8c**. **6g** was characterized by: $^1$H-NMR ($CDCl_3$, δ ppm, *J* Hz): **5.69**(ddq, 1H, H-5, 2.3, 5.8, 8.1); **5.56**(dq, 1H, H-6, 2.3, 5.8); **3.62**(dd, 2H, H-7, 7.4, 10.5); **3.54**(m, 1H, H-8); **3.51**(dq, 1H, H-8, 7.0, 9.8); **3.24**(m, 1H, H-6a, 8.5, 2.1); **2.84**(m, 1H, H-3a); **2.29-2.12**(m, 4H, 2H-4,H-1-3); **1.65**(dt, 1H, H-2, 5.6, 12.4); **0.87**(s, 8H, $CH_3$); **0.73**(m, 1H, H-2, 12.4); **0.02**(s, 6H, $CH_3$), $^{13}$C-NMR ($CDCl_3$, δ ppm): **132.42; 131.50**(C-5); **130.24; 129.67; 128.23**(C-6); **64.52**; **64.40; 64.18** (C-7,C-8); **51.99; 51.63**(C-6a); **46.07; 45.99**(C-1); **45.34**(C-3); **42.14; 41.61**(C-3a); **33.17; 32.99**(C-4); **30.86; 30.65**(C-2), **25.84**($\underline{C}H_3)_3C$; **18.26** $(CH_3)_3\underline{C}$.

4.8. *(±)-(1α,3α,3aβ,6aβ-1(3)-(1-isobutoxy-ethoxymethyl)-3(1)-methanol-1,2,3,3a,4,6a-hexahydropentalene* **6h**

340 mg (2.02 mmoles) Diol **4**, were protected with 0.32mL (2.424mmoles) iso-butylvinylether in the conditions presented at 3.2., resulting 0.64g crude mixture of compound **8b** and **6h**, as slight yellow oil (Tlc, I, $R_{f8b}$=0.89, $R_{f\ 6h}$= 0.64), which was purified by pressure chromatography. There were obtained ~240 mg (~31.7%) pure **8b** and ~220 mg (~40.6%) pure **6h**, characterized by: $^1$H-NMR($CDCl_3$, δ ppm, J Hz): **5.70**(m, 1H, H-5); **5.55**(m, 1H, H-6); **4.63**(m, 1H, H-1'); **3.64-3.25**(m, 6H, H-7-8, 1H-3', H-6a); **3.14**(m, 1H, H-3'); **2.83**(m, 1H, H-3a); **2.31-2.13**(m, 4H, H-1-3, 2H-4); **1.81**(m, 1H, H-4'); **1.60**(m, 1H, syst. AB, H-2A); **1.26**(d, 3H, H-2', 5.6); **0.88**(dd, 6H, H-5',1.0, 6.7); **0.78**(q, 1H, syst. AB H-2B, 11.7), $^{13}$C-NMR($CDCl_3$, $\delta$ ppm): **132.13; 131.64**(C-5); **129.71; 129.66**(C-6); **100.10**; **99.91**(C-1'$_7$); **72.52; 72.17**(C-3'); **67.32; 66.43**(C-7); **64.28; 64.08**(C-8); **52.29; 52.-7; 51.81**(C-6a); **46.08; 45.43**(C-3); **43.48; 42.85**(C-1); **42.48; 42.24**(C-3a); **33.31; 33.05**(C-4); **31.89; 31.30**(C-2); **28.55**(C-4'); **19.66; 19.55**(C-2'); **19.25** (C-5').

## CONCLUSIONS

Starting from 5-exo,6-exo-dihydroxy-endo-3a,4,5,6,7,7a-hexahydro-4,7-methanoindene **1**, easily obtained by permanganate hydroxylation of *endo*-dicyclopentadiene, we obtained in high yield, in two steps, the hexahydropentalenedimethanol intermediate **4**, useful in synthesis of natural product analogues[1,2] and in fine organic synthesis. This stable, crystallized compound to be further functionalized on the double bond or on the exocyclic hydroxymethyl groups was protected to one or to both hydroxyl groups obtaining mono-protected derivatives **6a-h** and the corresponding bis-protected derivatives with acyl- (**5a-e, 7**), ether- (**8a-b**) and *tert*-butyldimethylsilyl ether (**8c**)-protecting groups The compounds were investigated by elemental analysis, IR, $^1$H- and $^{13}$C-NMR spectra or some of these and also MS for the compound **4**, confirming their structure.

## REFERENCES


1. C.I. Tănase, F.G. Cocu, M.T. Căproiu and C. Drăghici, *Rev. Chim., (English Edition)*, **2001**, *2*, 11.
2. C.I. Tănase, F.G. Cocu, M.T. Căproiu and C. Drăghici, *RO-patent-116896*, **2001**.
3. C.I. Tănase, *Thesis*, Polytechnical University Bucharest, 1997.
4. a). Y. Chow, *J.Chem.Soc., Perkin Trans I*, **1982**, 1419.; b). Y. Chow and H. Richard, *J.Chem.Soc., Perkin Trans I,* **1982**, 1405.
5. a). D. Brewster, M.Myers, J. Ormerod, M.E. Spinner and S. Turner, A.C.B. Smith, *J.Chem.Soc., Chem.Commun.,* **1972**, 1235. b). D. Brewster, M.Myers, J. Ormerod, P. Otter, A.C.B. Smith, M.E. Spinner and S. Turner, *J.Chem.Soc.,Perkin Trans. I*, **1973**, 2796.
6. a) T. Ogino, *Tetrahedron Lett.,* **1980**, *21*, 177; b) T. Ogino and K. Mochizuki, *Chem.Lett,* **1979**, 443.
7. G.A. Tolstikov, M.S. Miftakov, N.A. Danilova and O.V. Sitikova, *Zhur.Org.Kim* . **1985**, *XXI*, 675.
8. C.I. Tănase and F.G.Cocu, unpublished results.
9. C.-P.Chang, L.-F. Hsu and N.-C. Chang, *J. Org. Chem.,* **1994**, *59*, 1898.