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# A VERSATILE REGIO- AND STEREOSPECIFIC ANNULATION METHOD - III.

## PREPARATION OF SUBSTITUTED DERIVATIVES OF cis-BICYCLO[3.3.0]OCTANES, cis-BICYCLO[4.3.0]NONANES AND cis-BICYCLO[4.4.0]DECANES

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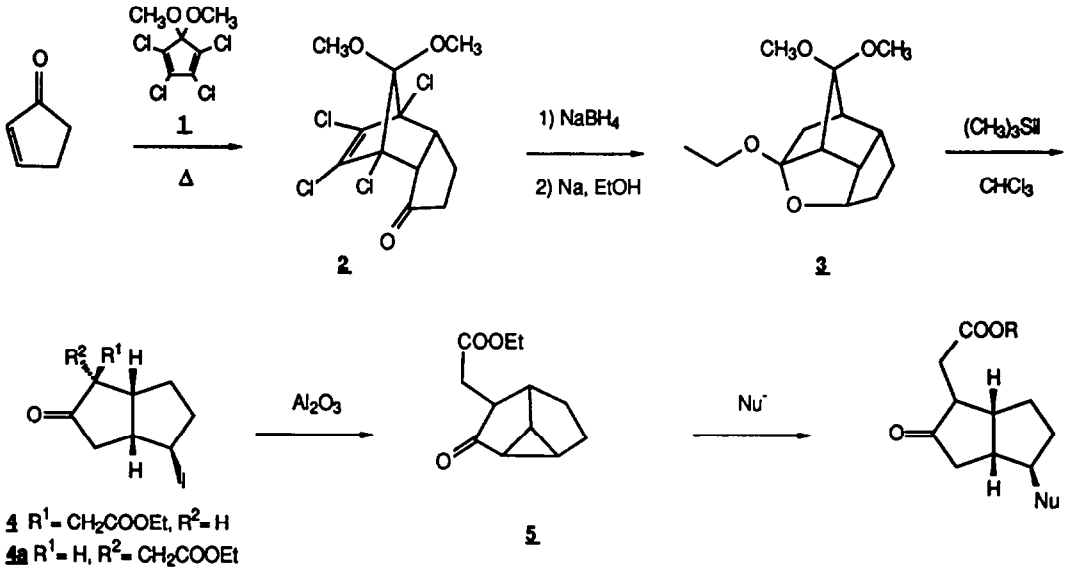
*Abstract:* The applicability of the recently developed annulation method[1,2] is demonstrated by the construction of regio- and stereospecifically substituted fused ring systems.

**Introduction :** Recently we developed an annulation method[1,2] starting with cycloaddition of allylically heterosubstituted olefins with 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene **1**. Further conversion of the cycloadducts led to doubly bridged intermediates, which by acidic fragmentation yielded either the stereo- and regiospecifically substituted five or six-membered ring systems, depending on solvent, Lewis acid and (additional) nucleophile.

To demonstrate the usefulness of this method for more complex systems, we have prepared regiospecifically substituted cis-fused ring systems, which might be used as intermediates in the syntheses of a variety of important groups of natural products with physiological activity.

**Preparation of regiospecifically substituted cis-bicyclo[3.3.0]octanes:** Bicyclo[3.3.0]octanes are part of structures of secondary metabolites [3], which possess a variety of physiologically interesting effects in mammals. They are also intermediates in the synthesis of iridoids, a large group of compounds found in plants and insects, which exhibit physiological effects in mammals[4]. It is therefore of importance to be able to choose from several convenient methods to prepare these intermediates[5].

Starting with **1** and 2-cyclopentenone the tricyclic ketone **2** was produced. Reduction with sodium borohydride yielded stereoselectively the endo alcohol , which by treatment with sodium in ethanol at reflux led to the tetracyclic diketal **3**[1]. Iodotrimethylsilane in chloroform[6] transformed this highly strained compound into bicyclo[3.3.0]octane **4** and a small amount of its diastereomer **4a** (epimer configuration at C-2') in good yield.




scheme 1

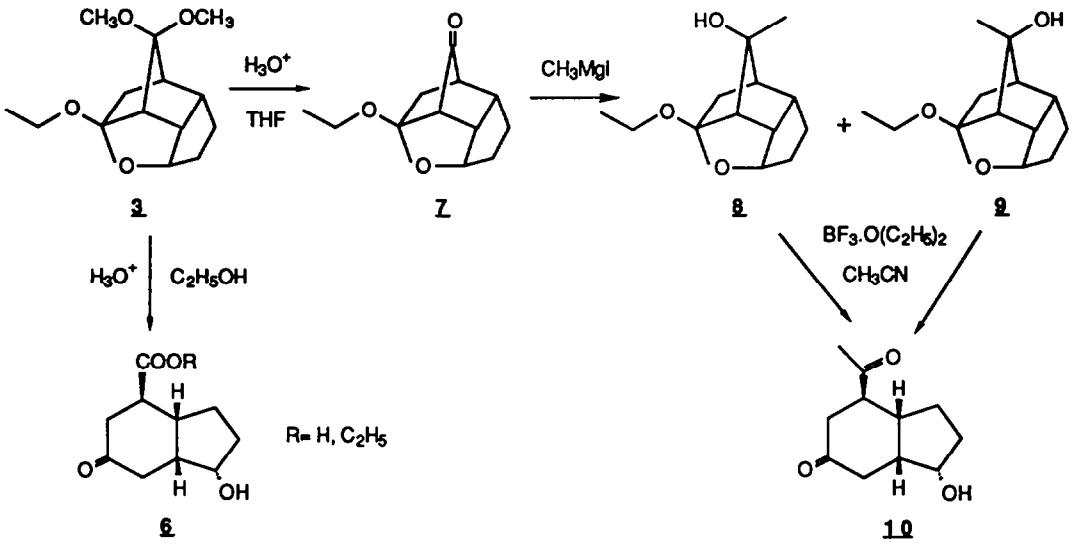
The structure determination of **4** was based on IR- and $^{13}$C-NMR spectroscopic data, which established the cyclopentanone moiety; the ester group as well as the secondary iodide were revealed by $^{1}$H-NMR-, $^{13}$C-NMR-, and mass spectroscopic data.

Treatment of a 19 : 1 as well as a 4 : 1 mixture of **4** and its diastereomer **4a** under the reaction conditions mentioned above led in each case to a 8 : 1 mixture of **4** and its stereoisomer **4a**, thus explaining the existence of the diastereoisomer **4** in the original reaction mixture as the product of a subsequent epimerization. Alumina transformed these mixture of stereomeric bicyclo[3.3.0]octanes in high yields into the tricyclic compound **5**. The spectral data were consistent with loss of the secondary iodide. Formation of cyclopropane was easily explained by generation of the enolate of **4** with alumina and subsequent intramolecular nucleophilic substitution of the iodide. The $^{1}$H-NMR-, MS- and IR spectroscopic properties correlated well with those reported of tricyclo[3.3.0.0$^{2,8}$]octan-3-one[7a]. Most notable was the base peak at *m/e*= 80 in the MS spectra of both substances, which Monti[7a] explained as loss of a ketene moiety from the molecule. Several synthetic routes to tricyclo[3.3.0.0$^{2,8}$]octan-3-ones have been reported[7]. Authors of these publications showed that the cyclopropyl moiety is easily cleaved regio- and stereoselectively by nucleophiles due to the vicinal keto group[8]. Thus preparation of a very versatile building block[9] for the synthesis of naturally occurring polyquinanes and iridoids is now very conveniently achieved.

**Preparation of regiospecifically substituted tetrahydro- and cis-hexahydroindanones:** cis-Bicyclo[4.3.0]nonanes are building blocks for a variety of natural products; for example the lycopodium alkaloids of the magellan-fawcettimin-type[10], the tutinanolides[11], the alliacolides[12], and the antibiotic ikarugamycin[13]. We therefore intended to synthesize cis-bicyclo[4.3.0]nonane derivatives with varying

substitution pattern.

Treatment of tetracycle **3** with diluted aqueous HCl in ethanol yielded the bicyclo[4.3.0]nonane derivatives **6** as described previously[2].

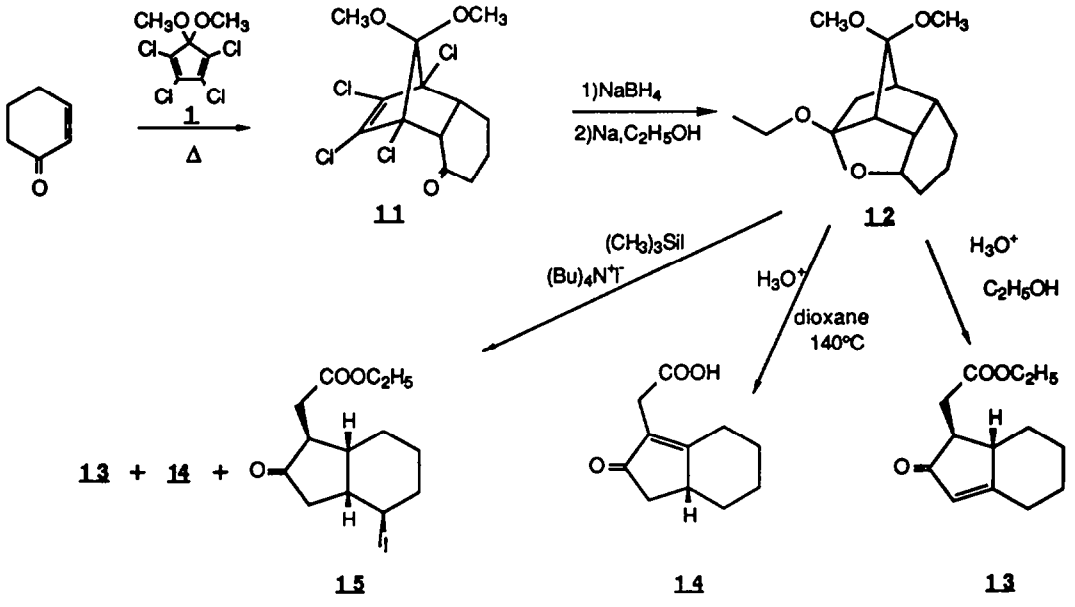



scheme 2

To obtain differently acyl substituted indanone derivatives the dimethoxyketal **3** was hydrolyzed to the monoketone **7**[2]. This ketone was then transformed to a 5 : 3 mixture of the tertiary alcohols **8** and **9** by treatment with methyl magnesium iodide. The syn and anti orientations of the hydroxy group in **8** and **9** were determined by difference nuclear Overhauser effects. The best way to fragment these products was by treatment with boron trifluoride etherate in acetonitrile. The high tendency of the reaction products for aldolization was circumvented by employing diluted reaction solutions. Under these conditions both alcohols could be transformed to the methylketone **10** in excellent yields.

Indanones with quite different substitution patterns were obtained by starting with the tetracycle **12**, which was prepared as described previously[1] by cycloaddition of 2-cyclohexenone and **1** yielding ketone **11**. Stereoselective reduction to the corresponding alcohol and subsequent treatment with sodium in ethanol at reflux transformed **11** into **12**. Fragmentation in acidic aqueous ethanol led mainly to the tetrahydroindanone derivate **13**[2].

By treatment with sodium ethoxide, product **13** was converted to the ethyl ester of **14**. Acid **14** was more effectively prepared by treatment of **12** in dioxane/water with a trace amount of acid at 140°C. Structure determination of **14** relied mainly on the UV spectrum, on the singlet for the two protons at C-2 in the $^1$H-NMR spectrum, the position of the signals of the carbonyl, and the olefinic carbon atoms in the $^{13}$C-NMR spectrum.

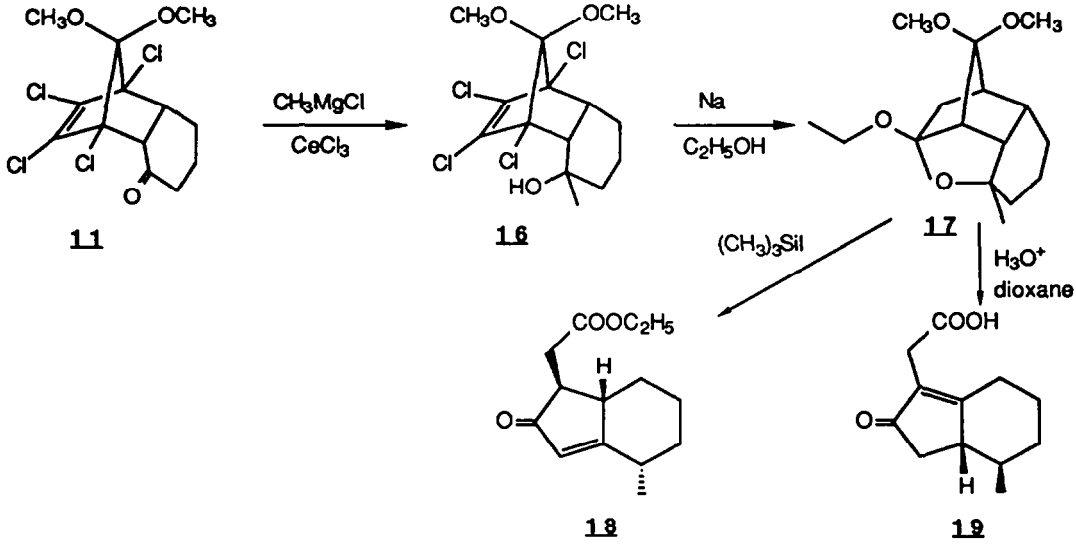



scheme 3

The difference in fragmentation behaviour between compound **3** (scheme 2) and **12** may be due to the exact antiperiplanar position of the proton attached at C-8 with respect to the C(1)-O bond in case of **12**,a geometrical requirement not as equally well satisfied in **3**.

By switching to an aprotic solvent, iodotrimethylsilane and an excess of tetrabutylammonium iodide at room temperature, the hexahydroindanone derivative **15** was obtained as the main product. Thus most of the stereocenters were conserved and a secondary iodo group was introduced. The lack of absorption in the UV region above 220nm as well as the signals of the carbonyl group in the $^{13}$C-NMR and the IR spectra were in accordance with a cyclopentanone moiety. The mass spectrum showed that the molecule contained iodine, which was confirmed by a proton signal at 3.98ppm. The coupling constant ($J_{1',2'}$= 11.5Hz) indicated axial attack by the iodide at C-2'in $S_N2$ fashion. The configuration at C-7' remained to be determined. The coupling constants of the proton attached to C-7' pointed to a half chair conformation of the cyclopentanone with antiperiplanar position of the protons at C-6' and C-7'.That was conclusive of epimerization at C-7' after the fragmentation. Contrary to compound **4**, treatment of **15** with alumina did not effect formation of a cyclopropylketone derivative . Use of DBU as base transformed **15** into a stereoisomeric mixture of ethyl 7-oxotricyclo[4.3.1.$0^{5,9}$]decan-10-yl carboxylates by intramolecular alkylation at the α-position of the acetate moiety. Efforts to separate this mixture have been to no avail.

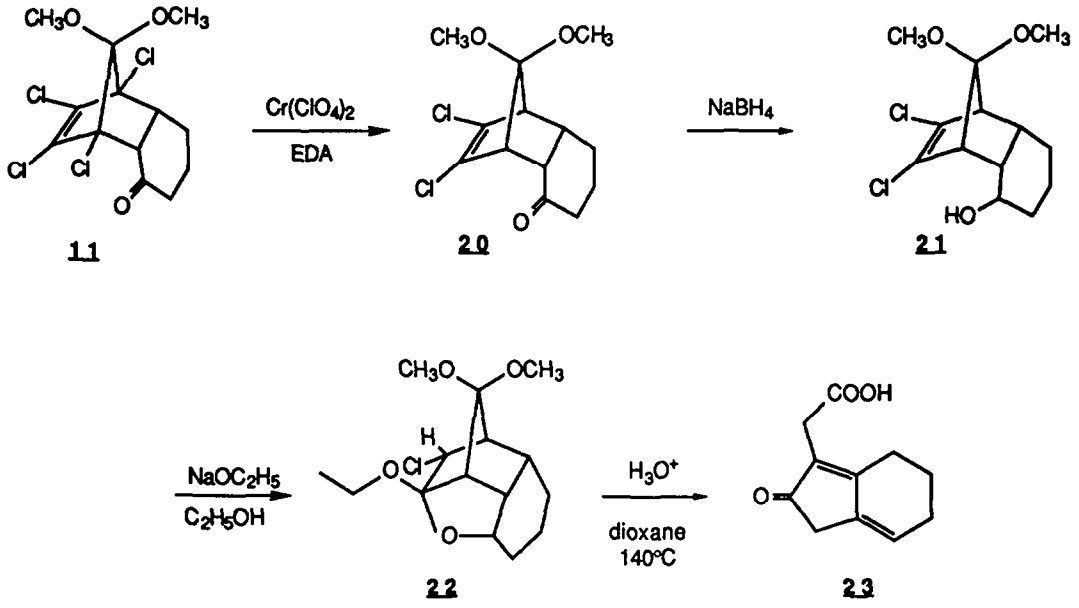
To introduce an alkyl substituent at C-2 of the indan-8-one derivatives, as found in the oplopanones[14], 11 was treated with methyl magnesium iodide. Contrary to compound 2 the desired tertiary alcohol was not obtained by these means[15]. To suppress enolization, ketone 11 was treated with a cerium reagent[16], prepared by treatment of methyl magnesium chloride with $CeCl_3$[17]. Under these conditions the tertiary alcohol 16 was formed quantitatively. Cyclization and dechlorination of 16 was achieved by sodium in ethanol at reflux. The resulting tetracycle 17 was converted to the tetrahydroindanone derivative 18 in good yield with aqueous acid in ethanol at reflux. Treatment by chlorotrimethylsilane and sodium iodide in acetonitrile at room temperature was equally effective. By analogy with compound 12, treatment of 17 with traces of aqueous HCl in dioxane/water at 140°C yielded the bicyclo[4.3.0]nonenone 19.




11 16 17 18 19

scheme 4

With compound 11 a further attempt to vary the substitution pattern was examined. 11 was partially dechlorinated with complexed chromium-II-salts[18]. By this method the bridgehead chlorines were exchanged for hydrogen yielding ketone 20, which was selectively reduced with sodium borohydride to afford 21. Treatment of 21 with sodium ethoxide in ethanol at reflux led to the monochlorinated tetracycle 22, which was transformed to the bicyclic dienone 23 by heating in dioxane/water with a trace amount of aqueous HCl in a sealed tube at 140°C. The unstable acid 23 was characterized as its methyl ester 24. The UV-spectrum was consistent with a substituted dienone with an exo and an endo cyclic double bond in a five membered ring. IR-, $^1$H-NMR-, $^{13}$C-NMR-, and mass spectroscopy confirmed this assumption.

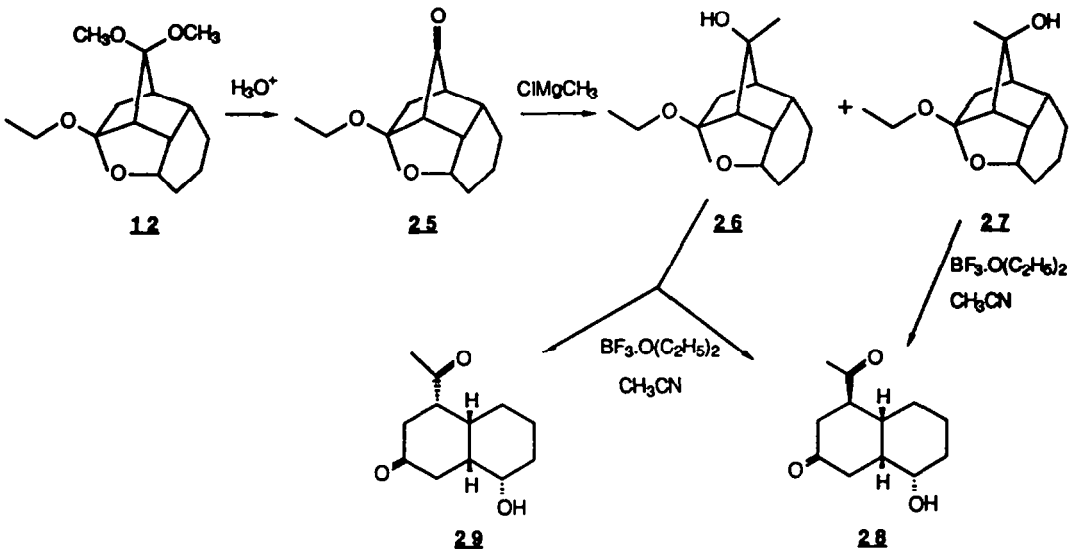



11 20 21 22 23

scheme 5

**Preparation of cis-bicyclo[4.4.0]decanones:** A variety of sesquiterpenes[11b] contains the cis-decaline system. Therefore high yielding methods to prepare stereospecifically substituted decalinones are desirable. Although certain cis-decalins are easily prepared by the Diels-Alder reaction or by hydrogenation of naphthalenes, the special substitution pattern which is rendered by our new method is not so conveniently accessible by other routes.

To achieve fragmentation to the decalinones, compound 12 had to be transformed to the ketone 25 by hydrolysis, and subsequently to the tertiary alcohols 26 and 27 by treatment with Grignard reagent. These alcohols were treated with boron trifluoride etherate in acetonitrile. The two alcohols differed in the rate of fragmentation. The syn alcohol 26 had to be treated at room temperature, which led to partial epimerization at C-2 of the originally produced bicycle 28, whereas the anti alcohol 27 fragmented at 0°C without epimerization to the decalinone derivative 28.




scheme 6

## Experimental

General notes: $^{1}$H-NMR- and $^{13}$C-NMR spectra were recorded on a Bruker Spectrospin WM 250 (250 MHz). Tetramethylsilane served as internal standard. Mass spectra were recorded on a spectrometer CH-7(Varian) and IR spectra on a Perkin Elmer 377 spectrometer. No IR spectra are given for substances without significant bands. Melting points were obtained using a Reichert "Kofler" hot stage microscope and are uncorrected. Adsorption chromatography was conducted on silica gel (70-230 mesh ASTM, Merck) or aluminium oxide 90 standardized acc. to Brockmann (70-230 mesh ASTM, Merck). Silica gel (230-400 mesh ASTM, Merck) was used for flash chromatography.

The preparation of compounds 2, 3, 6, 7, 11, 12, 13, and 25 is described in previous publications[1,2].

**(±)-(1'R*,2'S*,5'R*,6'R*)Ethyl-6'-iodo-3'-oxobicyclo[3.3.0]oct-2'-yl acetate (4):** To chloroform(abs.; 1.5ml) under an atmosphere of argon were added 2 drops of pentene and iodotrimethylsilane (0.16ml) and stirred at room temperature for 10 min. To this solution was added 3 (254mg; 1mmol), dissolved in chloroform(1ml), and stirred at room temperature for 15 min. After addition of aqu. $NaHCO_3$(5%; 5ml) the layers were separated . The org. layer was treated with $Na_2S_2O_3$ and the aqueous layer was extracted with chloroform several times. The org. layers were washed with brine, dried over

$MgSO_4$ and the solvent evaporated. Flash chromatography on silica gel with toluene : diethyl ether = 49 : 1 yielded a mixture of the diastereomers **4** and **4a** (250mg; 74%). By flash chromatography on silica gel with toluene : dichloromethane = 19 : 1 pure **4** was isolated next to mixtures of **4** and **4a**.

Epimerization: Treatment of a mixture of **4** and **4a** (19:1) as well as one of **4** and **4a** (4:1) under the above mentioned reaction conditions yielded in each case a mixture of **4** and **4a** (~8 : 1). The ratios were determined by $^1$H-NMR-spectroscopy. **IR($CCl_4$)($cm^{-1}$):** 1750sh, 1740. **$^1$H-NMR($CDCl_3$)(δ):** 1.26(t)(3H) $J_{1'',2''}$= 7Hz C-H(2"); 1.62(m)(1H) $w_{1/2}$= 26Hz C-H(8'endo); 2.1-2.5(m)(4H) C-H(2'), C-H(7'exo), C-H(7'endo), C-H(8'exo); ~2.5(m)(1H) $J_{1',5'}$= 9.5Hz C-H(1'); 2.26(dd)(1H) $J_{4',4'}$= 19Hz, $J_{4'endo,5'}$= 4Hz C-H(4'endo); 2.54(part A of an ABX system)(1H) $J_{2,2}$= 17Hz, $J_{2a,1'}$= 5.3Hz C-H(2a); 3.6(dd)(1H) $J_{4',4'}$= 19Hz, $J_{4'exo,5'}$= 9.5Hz C-H(4'exo); 2.68(part B of an ABX system)(1H) $J_{2,2}$= 17Hz, $J_{2b,1'}$= 5.3Hz C-H(2b); 3.03(m)(1H) $J_{5',6'}$= 8Hz, $J_{5',1'}$ ~ $J_{5',4'exo}$ = 9.5Hz, $J_{5',4'endo}$= 4Hz C-H(5'); 3.87(dt)(1H) $J_{6',5'}$= 8Hz, $J_{6',7'exo}$ = $J_{6',7'endo}$ = 6Hz C-H(6'); 4.13(q)(2H) $J_{1'',2''}$= 7Hz C-H(1"). **$^1$H-NMR($C_6D_6$)(δ):** 0.93(t)(3H) $J_{1'',2''}$= 7Hz C-H(2"); 0.9-1.06(m)(1H) C-H(8'endo); 1.42-1.93(m)(5H) C-H(1'), C-H(2'), C-H(7'exo), C-H(7'endo), C-H(8'exo); 1.76(dd)(1H) $J_{4',4'}$= 19Hz, $J_{4'endo,5'}$= 4Hz C-H(4'endo); 2.16(dd)(1H) $J_{4',4'}$= 19Hz, $J_{4'exo,5'}$= 9Hz C-H(4'exo); 2.23(part A of an ABX system)(1H) $J_{2,2}$= 17Hz, $J_{2a,1'}$= 6.5Hz C-H(2a); 2.46(part B of an ABX system)(1H) $J_{2,2}$= 17Hz, $J_{2b,1'}$= 5Hz C-H(2b); 2.5(m)(1H) $J_{5',4'exo}$= 9Hz, $J_{5',1'}$ = $J_{5',6'}$ = 8.5Hz, $J_{5',4'endo}$= 4Hz C-H(5'); 3.09(m)(1H) $J_{6',5'}$= 8.5Hz, $J_{6',7'exo}$ = $J_{6',7'endo}$ = 8Hz C-H(6'); 3.90(q)(2H) $J_{1'',2''}$= 7Hz C-H(1"). **$^{13}$C-NMR($CDCl_3$)(δ):** 14.2 C-2"; 30.2 C-6'; 31.9 C-7'; 34.3 C-8'; 39.5 C-2; 41.5 C-4'; 44.3 C-1'; 51,0 and 51.5 C-2'and C-5'; 60.7 C-1"; 171.6 C-1; 216.7 C-3'. **MS:** 336($M^+$)(0.15%), 291($M^+$-OEt)(18%), 209($M^+$-I)(44%), 163($M^+$-HI-OEt)(100%), 135($M^+$-HI-COOEt)(56%), 121($M^+$-HI-$CH_2$COOEt)(53%).

**(±)-(1'R*,2'S*,4'S*,5R*,8'S*)-Ethyl-3'-oxotricyclo[3.3.0.0$^{2',8'}$]oct-4'-yl acetate (5):** **4** and **4a** (161.3mg) was slowly chromatographed (within 4h) on alumina(9g)in petroleum ether : diethyl ether (6:1) yielding **5** (95.1mg; 95%). **IR($CCl_4$)($cm^{-1}$):** 3050, 1735. **$^1$H-NMR($CDCl_3$)(δ):** 1.27(t)(3H) $J_{1'',2''}$= 7Hz C-H(2"); 1.51-1.75(m)(2H) C-H(6'endo), C-H(7'endo); 1.86-2.16(m)(5H) C-H(2'), C-H(4'), C-H(6'exo), C-H(7'exo), C-H(8'); 2.40(dd)(1H) $J_{2,2}$= 16Hz, $J_{2a,4'}$= 10.5Hz C-H(2a); 2.55(dd)(1H) $J_{2,2}$= 16Hz, $J_{2b,4'}$= 5Hz C-H(2b); 2.59-2.75(m)(2H) C-H(1'), C-H(5'); 4.16(q)(2H) $J_{1'',2''}$= 7Hz C-H(1"). **$^{13}$C-NMR($CDCl_3$)(δ):** 14.2 C-2"; 25.2 C-6'; 31.8, 35.3 and 39.0 C-1', C-5'and C-8'; 37.3 C-7'; 40.6 C-2; 44.1 C-4'; 53.5 C-2'; 60.7 C-1"; 171.5 C-1; 216.6 C-3'. **MS:** 208($M^+$)(3.4%), 163($M^+$-OEt)(7%), 80($C_6H_8^+$)(100%).

**(±)-(1S*,3R*,5R*,6R*,7S*,8S*,9R*)-3-Ethoxy-6-methyl-2-oxatetracyclo[6.3.0.0$^{3,7}$0$^{5,9}$]undecan-6-ol (8) and (±)-(1S*,3R*,5R*,6S*,7S*,8S*,9R*)-3-ethoxy-6-methyl-2-oxatetracyclo-[6.3.0.0$^{3,7}$0$^{5,9}$]undecan-6-ol (9):** To a solution of methyl magnesium iodide(7mmol) in diethyl ether(abs.;10ml) was added **7**(1g; 5mmol) dissolved in diethyl ether(abs.,6ml), and the resulting solution refluxed for 2 h. The cooled reaction mixture was treated with aqu. sat. $NH_4Cl$ and four times extracted with dichloromethane. The org. layers were washed with brine, dried over $MgSO_4$, filtered and the solvent evaporated. Flash chromatography on silica gel with petroleum ether : acetone (11:1) yielded **8** (0.465g; 41.5%; m.p.85°C) and **9** (0.357g; 32%; m.p.63-66°C).

**8: IR($CCl_4$)($cm^{-1}$):** 3575, 3450br. **$^1$H-NMR($CDCl_3$)(δ):** 1.21(t)(3H) $J_{1',2'}$= 7.2Hz C-H(2'); 1.39(s)(3H) C(6)C-$H_3$; 1.5-2.1(m)(6H) C-H(10endo), C-H(11endo), C-H(10exo), C-H(11exo), C-H(5), O-H; 1.9(part A of an ABX system)(1H) $J_{4,4}$= 14Hz, $J_{4,5}$= 0Hz C-H(4endo); 2.22-2.38(m)(2H) $J_{4,4}$= 14Hz, $J_{4,5}$= 3.5Hz C-H(4exo), C-H(7); 2.7(m)(2H) C-H(9), C-H(8); 3.65( part A of an $ABX_3$ system)(1H) $J_{1',1'}$= 8Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 3.74(part B of an $ABX_3$ system)(1H) $J_{1',1'}$= 8Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 4.46(m)(1H) $J_{1,11}$= 3.5Hz, $J_{1,8}$= 3.5Hz C-H(1). **$^{13}$C-NMR($CDCl_3$)(δ):** 15.5 C-2'; 21.2 C(6)-$\underline{C}H_3$; 23.9 C-10; 35.9 C-11; 38.2 C-

4; 42.2 C-9; 47.5 C-5; 49.5 C-8; 55.4 C-7; 59.0 C-1′; 81.1 C-1; 86.9 C-6; 115.3 C-3. **MS:** 224($M^+$)(6%), 206($M^+$-$H_2O$)(24%), 136(13%),133(72%), 43(100%).

**9: IR($CCl_4$)($cm^{-1}$):** 3620, 3450br. **$^1$H-NMR($CDCl_3$)(δ):** 1.2(t)(3H) $J_{1',2'}$= 7.2Hz C-H(2′); 1.48(s)(3H) C(6)C-$H_3$; ~1.5(m)(1H) C-H(10endo); 1.74(m) (exchangeable with $D_2O$) O-H; 1.6-1.8(m)(3H) C-H(10exo),C-H(5), C-H(11exo); 1.85(part A of an ABX system)(1H) $J_{4,4}$= 13.5Hz, $J_{4,5}$= 0 C-H(4endo); 1.97(part B of an ABX system)(1H) $J_{4,4}$= 13.5Hz, $J_{4,5}$= 3.5Hz, $J_{4,9}$= 1Hz C-H(4exo); 2.06(dd)(1H) $J_{10endo,11}$= 8Hz, $J_{11,11}$= 12Hz C-H(11endo); 2.19(dd) $J_{7,8}$= 5Hz C-H(7); 2.98(m)(1H) $J_{8,9}$= 10Hz, $J_{8,7}$ ~5Hz, $J_{8,1}$= 4.5Hz C-H(8); 3.11(m)(1H) $J_{8,9}$= 10Hz, $J_{9,10exo}$= 10Hz, $J_{9,10endo}$= 4.5Hz, $J_{9,5}$= 4Hz C-H(9); 3.55(part A of an $ABX_3$ system)(1H) $J_{1',2'}$= 7.2Hz, $J_{1',1}$= 8.7Hz C-H(1′); 3.7(part B of an $ABX_3$ system)(1H) $J_{1',2'}$= 7.2Hz, $J_{1',1}$= 8.7Hz C-H(1′); 4.4(m)(1H) $J_{1,8}$= 4.5Hz, $J_{1,11exo}$= 3.8Hz C-H(1). **$^{13}$C-NMR($CDCl_3$)(δ):** 15.6 C-2′, 21.4 C(6)-$CH_3$, 22.7 C-10, 36.5 C-11, 38.4 C-4, 43.1 C-9, 47.2 C-5, 52.0 C-8, 55.3 C-7, 58.7 C-1′, 80.1 C-1, 87.6 C-6, 113.3 C-3. **MS:** 224($M^+$)(3%), 206($M^+$-$H_2O$)(35%), 151(8%), 136(14%), 133(78%), 43(100%).

**(±)-(1R*,2R*,6R*,7S*)-2-Acetyl-7-hydroxybicyclo[4.3.0]nonan-4-one (10):** To a solution of 8 or 9 resp.; (100mg; 0.44mmol) in dry acetonitrile (100ml) at 0°C was added $BF_3.OEt_2$ (8.5ml), and the mixture was stirred for 5 h. Then sat. aqu. $NaHCO_3$ was added and the mixture was extracted with dichloromethane. The org. layers were washed with brine, dried over $MgSO_4$, and the solvent evaporated. Flash chromatography on silica gel with diethyl ether : petroleum ether : ethyl acetate (6:1:1) yielded 10 (73mg; 84%) or, starting from 9, 10 (83mg; 95%) was obtained. **IR($CCl_4$)($cm^{-1}$):** 3620, 3440 br., 1710. **$^1$H-NMR($CDCl_3$)(δ):** 1.67(m)(1H) C-H(9); 1.88(m)(3H) C-H(8), C-H(9); 2.22(s)(3H) C-H(2′); 2.2-2.7(m)(7H) $J_{2,3exo}$= 11Hz, $J_{3exo,3endo}$= 16Hz C-H(1), C-H(3exo), C-H(3endo), C-H(5exo), C-H(5endo), C-H(6), O-H; 3.13(m)(1H) $J_{1,2}$= 9Hz, $J_{2,3exo}$= 11Hz, $J_{2,3endo}$= 4Hz C-H(2); 4.27(m)(1H) $J_{6,7}$= 3.5Hz, $J_{7,8exo}$= 3.5Hz, $J_{7,8endo}$= 3.5Hz C-H(7). **$^{13}$C-NMR($CDCl_3$)(δ):** 28.9 C-8; 29.5 C-2′; 34.2 C-9; 37.7 C-1; 38.2 and 40.5 C-3 and C-5; 43.2 C-6; 52.5 C-2; 75.1 C-7; 209.9 and 211.7 C-1′ and C-4. **MS:** 196($M^+$)(1.7%), 178($M^+$-$H_2O$)(5.9%), 153($M^+$-$CH_3CO$)(18%), 135($M^+$-$H_2O$-$CH_3CO$)(13%), 107($M^+$-$H_2O$-$CH_3CO$-CO)(18%), 93($M^+$-$H_2O$-$CH_3CO$-$CH_2CO$)(39%), 43($CH_3CO^+$)(100%).

**(±)-Bicyclo[4.3.0]non-6′-en-8′-on-7′-yl acetic acid (14):** 12 (420mg; 1.6mmol) was dissolved in dioxane(14.2ml) : water(2.8ml) : aqu. HCl(0.6N; 0.4ml) and heated in a sealed tube at 140°C for 68h. The solvent of this reaction mixture was evaporated, dichloromethane added and extracted with aqu. $NaHCO_3$. The aqueous layer was acidified and extracted with ethyl acetate. The org. layers were dried over $MgSO_4$ and the solvent evaporated. The resulting crystalline mass was recrystallized from petroleum ether : diethylether yielding 14 (150mg; 49.3%; m.p.: 127°C). **IR(KCl)($cm^{-1}$):** 3300-2200 br., 1740, 1735, 1675, 1635. **$^1$H-NMR($CDCl_3$)(δ):** 1.12(m)(1H) $J_{2',3'endo}$= 3.3Hz, $J_{2',2'}$= $J_{2',3'exo}$= $J_{2',1'}$= 12.5Hz C-H(2′endo); 1.37(m)(1H) $J_{4'endo,3'endo}$= $J_{4'endo,5'endo}$= 3.7Hz, $J_{4'endo,3'exo}$= $J_{4'endo,5'exo}$= $J_{4',4'}$= 12.7Hz C-H(4′endo); 1.53(m)(1H) $J_{3'exo,4'exo}$= $J_{3'exo,2'exo}$= 3Hz, $J_{3'exo,4'endo}$= $J_{3'exo,2'endo}$= $J_{3',3'}$= 13.0Hz C-H(3′exo); 1.86(m)(1H) $J_{3',3'}$= 13Hz, $J_{3'endo,4'endo}$= 3.7Hz, $J_{3'endo,2'endo}$= 3.3Hz, $J_{3'endo,4'exo}$ and $J_{3'endo,4'endo}$ ≤ 3Hz C-H(3′endo); 2.02(m)(1H) $J_{9',9'}$= 16.7Hz C-H(9′); 2.06(m)(1H) $J_{4',4'}$= 12.7Hz C-H(4′exo); 2.20(m)(2H) $J_{2',2'}$= 12.5Hz C-H(2′exo) and $J_{5',5'}$= 13Hz, $J_{5'exo,4'endo}$= 12.7Hz, $J_{5'exo,4'exo}$= 5.3Hz C-H(5′exo); 2.57-2.72(m)(2H) $J_{9',9'}$= 16.7Hz C-H(9′) and C-H(1′); 2.83(m)(1H) $J_{5',5'}$= 13Hz, $J_{5'endo,4'endo}$= 3.7Hz C-H(5′endo); 3.27(s)(2H) C-H(2); 8.74(br)(1H) COO-H. **$^{13}$C-NMR($CDCl_3$)(δ):** 24.4 C-3′; 26.6 C-4′; 28.2 C-2′; 29.2 C-5′; 35.0 C-9′; 40.9 C-1′; 41.1 C-2; 129.9 C-7′; 175.0 C-1; 180.5 C-6′; 208.1 C-8′. **MS:** 195(M+$H^+$)(10%), 194($M^+$)(73%), 176($M^+$-$H_2O$)(31%), 150($M^+$-$CO_2$)(81%), 148($M^+$-HCOOH)(100%). **UV:** $\lambda_{max}$(ethanol)= 236nm.

**(±)-(1′R*,2′R*,6′S*,7′S*)Ethyl-2′-Iodo-8′-oxobicyclo[4.3.0]non-7′-yl acetate (15):** To a solution of tetrabutyl ammonium iodide (1.38 g) in chloroform (abs.; 2 ml) under an atmosphere of argon were added 2 drops of pentene and iodotrimethylsilane (0.09 ml), and stirred at room temperature for 10 min. To this solution was added 12 (98 mg) dissolved in chloroform (0.5 ml). Stirring was continued at room temperature for 2 h, then sat. aqu. $NaHCO_3$ (4 ml) was added and the aqu. layer was extracted with chloroform. The org. layers were washed with sat. aqu. $Na_2S_2O_3$ and with brine, dried over $MgSO_4$, and the solvent evaporated. Flash chromatography on silica gel with petroleum ether : diethyl ether (6 :1) yielded 15 (66 mg; 52%; m.p.81°C), along with 13 (11 mg; 13%) and 14 (21 mg; 26%). **IR($CCl_4$)(cm$^{-1}$):** 1745, 1735. **$^1$HNMR($CDCl_3$)(δ):** 1.25(t)(3H) $J_{1'',2''}$= 7.1Hz C-H(2''); 1.44-1.57(m)(2H) C-H(4′); 1.66-1.87(m)(2H) C-H(5′); 2.10(m)(1H) $J_{3',3'}$= 13Hz, $J_{3'\beta,2'}$= 11.5Hz; $J_{3'\beta,4'\alpha}$= $J_{3'\beta,4'\beta}$= 7.5Hz C-H(3′β); 2.26(m)(1H) $J_{6',7'}$= 12.5Hz, $J_{6',1'}$= 6Hz, $J_{6',5'\alpha}$= 5.5Hz, $J_{6',5'\beta}$= 2.5Hz C-H(6′); 2.47(dd)(1H) $J_{2,2'}$= 17.3Hz, $J_{2a,7'}$= 7.3Hz C-H(2a); ~2.49(dd)(1H) $J_{3',3'}$= 13Hz, $J_{3'\alpha,2'}$= 4Hz C-H(3′α); 2.50(d)(2H) $J_{9',1'}$= 5Hz C-H(9′); ~2.64(m)(1H) $J_{7',6'}$= 12.5Hz, $J_{7',2a}$= 7.3Hz, $J_{7',2b}$= 4Hz C-H(7′); 2.64(dd)(1H) $J_{2,2'}$= 17.3Hz, $J_{2b,7'}$= 4Hz C-H(2b); 2.77(ddt)(1H) $J_{1',2'}$= 11.5Hz, $J_{1',6'}$= 6Hz, $J_{1',9'\alpha}$= $J_{1',9'\beta}$= 5Hz C-H(1′); 3.98(td)(1H) $J_{2',3'\beta}$= $J_{2',1'}$= 11.5Hz; $J_{2',3'\alpha}$= 4Hz C-H(2′); 4.14(q)(2H) $J_{1'',2''}$= 7.1Hz C-H(1''). **$^{13}$C-NMR($CDCl_3$)(δ):** 14.2 C-2''; 22.9 C-4′, 25.0 C-3′, 32.8 C-5′; 35.1 C-2′; 39.7 and 46.4 C-2 and C-9′; 42.4, 44.2 and 46.1 C-1′, C-6′ and C-7′; 60.8 C-1''; 171.8 C-1; 216.2 C-8′. **MS:** 305($M^+$-OEt)(7%), 223($M^+$-I)(16%), 177($M^+$-HI-OEt)(100%), 149($M^+$-HI-COOEt)(40%), 135($M^+$-HI-$CH_2$COOEt)(25%). High resolution mass spectrum: found: 350.038$^9$± 0.003$^5$, calc.: 350.037$^9$

**(±)-(1R*,2R*,3S*,7R*,8S*)-1,8,9,10-Tetrachloro-3-hydroxy-3-methyltricyclo[6.2.1.0$^{2,7}$]undec-9-en-11-one dimethylketal (16):** Anhydrous $CeCl_3$ (0.89 g) was stirred in THF (abs.; 9 ml) at room temperature under an atmosphere of argon for 2 h, cooled to 0°C, and methyl magnesium chloride (3 *M* in THF; 1.2 ml) was added. After stirring at 0°C for 2.5 h 11 (1.00 g), dissolved in tetrahydrofuran (abs.; 6 ml), was added. Stirring was continued at 0°C for additional 2 h, then aqu. acetic acid (0.6 ml in 15 ml water) was added. The mixture was extracted with chloroform, and the org. layers were washed with sat. aqu. $NaHCO_3$ and brine, and dried over $MgSO_4$. Evaporation of the solvent yielded crystalline 16 (1.03 g; 99%; m.p. 110 - 111°C). **IR($CCl_4$,cm$^{-1}$):** 3620. **$^1$H-NMR($CDCl_3$)(δ):** 1.2-1.8(m)(7H) C-H(4), C-H(5), C-H(6), O-H; 1.50(s)(3H) C(6)C-$H_3$; 2.55(d)(1H) $J_{2,7}$= 9Hz C-H(2); 2.71(m)(1H) C-H(7); 3.56(s)(3H) and 3.61(s)(3H) $OCH_3$. **$^{13}$C-NMR($CDCl_3$)(δ):** 17.3 and 17.7 C-5 and C-6; 31.7 $CH_3$; 35.5 C-4; 48.6 C-7; 51.6 $OCH_3$; 52.9 $OCH_3$; 53.5 C-2; 71.5 C-3; 78.3 and 78.6 C-1 and C-8; 112.9 C-11; 128.0 and 130.0 C-9 and C-10. **MS:** 339($M^+$-Cl)(26%), 303($M^+$-Cl-HCl)(13%), 253($M^+$-Cl-$(CH_2)_3$C(OH)$CH_3$) (100%).

**(±)-(1S*,3R*,5R*,7R*,8S*,9R*)-3-Ethoxy-1-methyl-2-oxatetracyclo[6.4.0.0$^{3,7}$.0$^{5,9}$]dodecan-6-one dimethylketal (17):** Sodium (8.6g; 370mmol) in small pieces was added to a solution of 16 (970mg; 2.6mmol) in ethanol (abs.; 35 ml) at reflux over 1 h. After the addition of sodium was finished heating at reflux was continued for 2 h. The cooled mixture was treated with crushed ice. The solution was extracted with dichloromethane. The org. layers were washed with brine, dried over $MgSO_4$, and the solvent evaporated. The crude product was distilled (Kugelrohr; 0.02mm) yielding 17 (650mg; 89%).

**$^1$H-NMR($CDCl_3$)(δ):** 1.24(m)(7H) $J_{1',2'}$= 7.2Hz C-H(2′), C(1)C-$H_3$, C-H(11endo); 1.40(m)(1H) and 1.71(m)(4H) C-H(10), C-H(11exo), C-H(12); 2.06(m)(1H) $J_{4exo,5}$= 3Hz, $J_{4endo,5}$= 0Hz, $J_{5,7}$= 1.5Hz, $J_{5,9}$= 3Hz C-H(5); 2.13(m)(3H) $J_{4exo,5}$= 3Hz, $J_{4endo,5}$= 0Hz, $J_{7,8}$= 5Hz, $J_{8,9}$= 9Hz C-H(4exo), C-H(4endo), C-H(8); 2.39(m)(1H) $J_{5,9}$= 3Hz, $J_{8,9}$= 9Hz, $J_{9,10\alpha}$= 9Hz, $J_{9,10\beta}$= 3Hz C-H(9); 2.89(dd)(1H) $J_{5,7}$= 1.5Hz, $J_{7,8}$= 5Hz C-H(7); 3.24(s)(3H) $OCH_3$; 3.27(s)(3H) $OCH_3$; 3.53(m)(1H) and 3.76(m)(1H) $J_{1',2'}$= 7.2Hz, $J_{1'\alpha,1'\beta}$= 9.4Hz C-H(1′). **$^{13}$C-NMR($CDCl_3$)(δ):** 15.6 C-2′; 18.4 C-11; 23.8 C-10; 29.4 C(1)$\underline{C}H_3$; 31.8 C-9; 34.5 C-12;

39.8 C-4; 44.2 C-8; 45.1 C-5; 48.7 C-7; 47.7 O<u>C</u>H$_3$; 50.6 O<u>C</u>H$_3$; 58.4 C-1′;76.9 C-1; 111.6 and 113.1 C-3 and C-6. **MS:** 282($M^+$)(2.3%), 251($M^+$-$OCH_3$)(100%).

**(±)-(2′S*,6′S*,7′S*)Ethyl-2′-methyl-8′-oxobicyclo[4.3.0]non-9′-en-7′-yl acetate (<u>18</u>):** <u>17</u>(99mg; 0.35mmol) was treated with a solution of sodium iodide(53mg; 0.70mmol) in acetonitrile(2ml) containing traces of 2,6-di-tert.butyl-4-methylphenol. Under an atmosphere of nitrogen chlorotrimethylsilane(44µl; 0.70mmol) was added, and the solution was stirred for 1h at room temperature. Water (2ml) was added and the mixture was extracted with diethyl ether. The ether layers were washed with sat. aqu. $NaHCO_3$, sat. aqu. $Na_2S_2O_3$ and brine, dried over $MgSO_4$ and the solvent evaporated. The crude product was purified by flash chromatography on silica gel with petroleum ether : diethyl ether (6:1) yielding <u>18</u> (58mg; 70%). **IR($CCl_4$)($cm^{-1}$):** 1740, 1710, 1620. **$^1$H-NMR($CDCl_3$)(δ):** 1.23(m)(8H) $J_{1'',2''}$= 7Hz, $J_{1'',2''}$= 7Hz, $J_{3'endo,3'exo}$= 13Hz, $J_{3'endo,4'exo}$= 13Hz, $J_{2',3'endo}$= 13Hz, $J_{3'endo,4'endo}$= 3.5Hz C-H(1″), C-H(2″), C-H(3′endo), C-H(5′endo); 1.60(m)(1H) $J_{3'endo,4'exo}$= 13Hz, $J_{4'exo,4'endo}$= 13Hz, $J_{4'exo,5'endo}$= 13Hz, $J_{3'exo,4'exo}$= 3.5Hz, $J_{4'exo,5'exo}$= 3.5Hz C-H(4′exo); 1.90(m)(1H) $J_{3'endo,4'endo}$= 3.5Hz, $J_{3'exo,4'endo}$= 3.5Hz, $J_{4'exo,4'endo}$= 13Hz, $J_{4'endo,5'endo}$= 3.5Hz, $J_{4'endo,5'exo}$= 3.5Hz C-H(4′endo); 2.05(m)(1H) $J_{3'endo,3'exo}$= 13Hz, $J_{3'exo,4'exo}$= 3.5Hz, $J_{3'exo,4'endo}$= 3.5Hz, $J_{2',3'exo}$= 3.5Hz C-H(3′exo); 2.47(m)(5H) $J_{2\alpha,2\beta}$= 15Hz, $J_{2\beta,7'}$= 9Hz C-H(2β), C-H(2′), C-H(5′exo), C-H(6′), C-H(7′); 2.87(dd)(1H) $J_{2\alpha,7'}$= 3Hz, $J_{2\alpha,2\beta}$= 15Hz C-H(2α); 4.19(q)(2H) $J_{1'',2''}$=7Hz C-H(1″); 5.92(m)(1H) C-H(9′). **$^{13}$C-NMR($CDCl_3$)(δ):** 14.2 C-2″; 18.0 C-1″; 25.3 C-4′; 34.6 C-5′; 35.0 and 35.8 C-2 and C-3′; 36.4 C-2′; 49.0 and 49.6 C-6′ and C-7′; 60.6 C-1″; 123.8 C-9′; 172.2 C-1; 187.0 C-1′; 208.0 C-8′. **MS:** 236($M^+$)(68%), 191($M^+$-OEt)(56%), 190($M^+$-EtOH)(60%), 163($M^+$-CO-OEt)(40%), 162($M^+$-CO-EtOH)(100%). **UV:** $\lambda_{max}$(ethanol) = 232nm.

**(±)-(1′S*,2′R*)-2′-Methyl-8′-oxobicyclo[4.3.0]non-6′-en-7′-yl acetic acid (<u>19</u>):** <u>17</u> (77mg; 0.27mmol) was dissolved in dioxane (2.5ml) : aqu. HCl (2%; 0.4ml) and heated in a sealed tube at 140°C for 24h. Then dichloromethane was added and the solution extracted with aqu. $NaHCO_3$ . The aqu. layers were acidified and extracted with dichloromethane. After washing with brine the organic solution was dried over $MgSO_4$ and the solvent evaporated yielding <u>19</u> (48mg; 85%) as a colourless oil. **IR($CCl_4$) ($cm^{-1}$):** 3600-2300br., 1740sh, 1710, 1660. **$^1$H-NMR($CDCl_3$)(δ):** 1.03(d)(3H) $J_{1'',2'}$= 6Hz C-H(1″); 1.28(m)(2H) C-H(2′), C-H(3′exo); 1.46(m)(1H) $J_{3'exo,4'endo}$= 13Hz, $J_{4'endo,5'exo}$= 13Hz, $J_{4'endo,4'exo}$= 13Hz, $J_{3'endo,4'endo}$= 3Hz, $J_{4'endo,5'endo}$=3Hz C-H(4′endo); 1.83(m)(1H) $J_{3'endo,3'exo}$= 9Hz C-H(3′endo); 2.08(m)(3H) $J_{4'exo,4'endo}$= 13Hz, $J_{4'exo,5'exo}$= 5Hz, $J_{4'endo,5'exo}$= 13Hz, $J_{5'exo,5'endo}$= 13Hz, $J_{1',9'exo}$= 2Hz, $J_{9'exo,9'endo}$= 19Hz C-H(4′exo), C-H(5′exo), C-H(9′exo); 2.25(m)(1H) $J_{1',2'}$= 8.5Hz, $J_{1',9'exo}$= 2Hz, $J_{1',9'endo}$= 6.5Hz C-H(1′); 2.61(dd)(1H) $J_{1',9'endo}$= 6,5Hz, $J_{9'exo,9'endo}$= 19Hz C-H(9′endo); 2.80(m)(1H) $J_{5'exo,5'endo}$= 13Hz C-H(5′endo); 3.25(m)(2H) C-H(2); 7.0(s)(1H) COO-H. **$^{13}$C-NMR($CDCl_3$)(δ):** 20.8 C-1″; 26.2 C-4′; 28.6 and 29.6 C-3′ and C-5′; 34.0 C-9′; 39.7 C-2; 40.7 C-2′, 47.7 C-1′; 130.7 C-7′; 175.4 C-1; 179.7 C-6′; 208.6 C-8′. **MS:** 208($M^+$)(36%), 191($M^+$-OH)(15%),190($M^+$-$H_2O$)(36%), 162($M^+$-$H_2O$-CO)(74%). **UV:** $\lambda_{max}$(ethanol)= 239nm.

**(±)-(1S*,2S*,7R*,8R*)-9,10-Dichloro-11-dimethoxytricyclo[6.2.1.0$^{2,7}$]undec-9-en-3-one (<u>20</u>):** Under an atmosphere of argon a freshly prepared solution of $Cr(ClO_4)_2$ (from 2.31g chromium powder, 7.7ml 70% $HClO_4$, and 47 ml $H_2O$; 44mmol) was added to a solution of ethylene diamine (11ml) in DMF (445ml). To this mixture a solution of <u>11</u> (2.0g; 5.5mmol) in DMF (10ml) was added and stirred at room temperature for 24 h. Then additional ethylene diamine (33ml) was added followed by a freshly prepared solution of $Cr(ClO_4)_2$ (from 6.94g chromium powder, 23ml 70% $HClO_4$, and 100ml $H_2O$; 133mmol). Stirring was continued for 72 h. Then the mixture was extracted with benzene, and the org. layer was washed

successively with hydrochloric acid (5%), sat. aqu. $NaHCO_3$, and sat. aqu. ammonium acetate, dried over $MgSO_4$ and the solvent evaporated. Flash chromatography on silica gel with toluene : ethyl acetate (99:1) yielded **20** (0.90g; 56%). **IR($CCl_4$)($cm^{-1}$):** 1710, 1610. **$^1$H-NMR($CDCl_3$)(δ):** 1.09(m)(1H) $J_{6,6}$= $J_{6,5exo}$≈$J_{6,7}$= 12Hz, $J_{6,5endo}$≈ 3Hz C-H(6endo); 1.74(m)(1H) $J_{5,5}$≈$J_{5,6endo}$≈$J_{5,4endo}$≈ 13Hz C-H(5exo); 1.85(m)(1H) C-H(5endo); 2.0(m)(1H) C-H(6exo); 2.06(m)(1H) $J_{4,4}$= 18Hz, $J_{4,5exo}$= 11Hz, $J_{4,5endo}$= 6.7Hz C-H(4endo); 2.43(m)(1H) $J_{4,4}$= 18Hz C-H(4exo); ~3.0(m)(1H) C-H(7); 3.04(m)(1H) $J_{1,8}$= 1.5Hz; $J_{8,7}$≈ 3Hz C-H(8); 3.09(m)(1H) $J_{1,2}$= 3.5Hz, $J_{2,7}$= 9Hz C-H(2); 3.20(s)(3H) OC-$H_3$; 3.21(s)(3H) OC-$H_3$; 3.42(dd)(1H) $J_{1,2}$= 3.5Hz, $J_{1,8}$= 1.5Hz C-H(1). **$^{13}$C-NMR($CDCl_3$)(δ):** 21.1 C-5; 25.6 C-6; 39.3 C-4; 40.3 C-7; 49.7 O<u>C</u>$H_3$; 50.0 C-2; 52.1 O<u>C</u>$H_3$; 54.9 C-8; 57.3 C-1; 115.2 C-11; 129.2 and 129.25 C-9 and C-10; 211.3 C-3. **MS:** 292($M^+$)(25%), 290($M^+$)(34%), 257($M^+$-Cl)(35%), 255($M^+$-Cl)(100%), 229(11%), 227(35%), 221(26%), 219(43%), 125(21%), 75(35%), 74(18%),59($COOCH_3$)(100%).

**(±)-(1S*,2S*,3S*,7R*,8R*)-9,10-Dichloro-3-hydroxytricyclo[6.2.1.0$^{2,7}$]undec-9-en-11-one dimethylketal (21):** **20** (820mg) was dissolved in methanol (50mg) and cooled to 0°C. After addition of sodium borohydride (250mg) the reaction mixture was stirred at 0°C for 3h. Addition of water was followed by extraction with dichloromethane for five times. The org. layers were washed with brine, dried over $MgSO_4$ and the solvent evaporated. The reaction mixture was purified by flash chromatography on silica gel with petroleum ether : diethylether (3:1) yielding **21** (722mg; 88%). **IR($CCl_4$)($cm^{-1}$):** 3610, 3500br., 1610. **$^1$H-NMR ($CDCl_3$)(δ):** ~1.35(m)(3H) C-H(4), C-H(5), C-H(6); 1.66(m)(4H) C-H(4), C-H(5), C-H(6), O-H; 2.58(m)(2H) C-H(2), C-H(7); 2.96(m)(1H) $J_{8,7}$≈ $J_{8,1}$≈ 2.5Hz C-H(8); 3.08(m)(1H) $w_{1/2}$= 6.5Hz C-H(1); 3.17(s)(3H) OC-$H_3$; 3.21(s)(3H) OC-$H_3$; 4.09(m)(1H) $w_{1/2}$= 16Hz C-H(3). **$^{13}$C-NMR($CDCl_3$)(δ):** 19.5 C-5; 22.9 C-6; 29.8 C-4; 38.1 C-7; 41.5 C-2; 49.5 O<u>C</u>$H_3$; 52.0 O<u>C</u>$H_3$; 55.4 C-8; 57.7 C-1; 69.0 C-3; 116.2 C-11; 128.4 and 128.8 C-9 and C-10. **MS:** 294($M^+$)(43%), 292($M^+$)(66%), 259($M^+$-Cl)(22%), 257($M^+$-Cl)(60%), 221(26%), 219(41%), 165(22%), 91(20%), 75(68%), 74(25%), 59(100%).

**(±)-(1S*,3S*,4R*,5R*,7S*,8S*,9R*)-4-Chloro-3-ethoxy-2-oxatetracyclo[6.4.0.0$^{3,7}$.0$^{5,9}$]dodecan-6-one dimethylketal (22):** Sodium (7g) was added to ethanol (abs.; 80ml) at reflux and stirred at reflux until the sodium was converted to sodium ethoxide. A solution of **21** (700mg) in ethanol (abs; 20ml) was added and stirring at reflux was continued for 2 h. The cooled reaction mixture was treated with ice and extracted six times with $CH_2Cl_2$. The org. layers were washed with brine, dried over $MgSO_4$ and the solvent evaporated. The reaction mixture was distilled (Kugelrohr; 0.02mm 150-170°C) and the resulting **22** (697mg; 96%) was recrystallized from pentane at -15°C (m.p. 67-69°C). **$^1$H-NMR($CDCl_3$)(δ):** 1.24(t)(3H) $J_{1',2'}$= 7.2Hz C-H(2'); ~1.3(m)(1H) C-H(11endo); 1.41(m)(1H) $J_{12,11}$= 5Hz, $J_{12,12}$= 12.3Hz, $J_{12,1}$= 2.5Hz C-H(12endo); 1.64(m)(1H) $J_{10,10}$= 15Hz, $J_{10,9}$≈ $J_{10,11}$≈ 11Hz, $J_{10,11}$= 6Hz C-H(10exo); 1.98(m)(2H) C-H(10endo) and C-H(12exo); 2.26 - 2.47(m)(3H) C-H(5), C-H(8), and C-H(11exo); 2.59(m)(1H) $J_{9,10exo}$= $J_{9,8}$= 10.5, $J_{9,5}$≈ $J_{9,10endo}$≈ 3.3Hz, $J_{9,4}$≈ 1Hz, $J_{9,7}$≈ 1.5Hz C-H(9); 2.83(dd)(1H) $J_{7,8}$= 5Hz, $J_{7,9}$≈ 1.5Hz C-H(7); 3.23(s)(3H) OC-$H_3$; 3.27(s)(3H) OC-$H_3$; 3,58(part A of an $ABX_3$ system)(1H) $J_{1',1'}$= 9Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 3.79(part B of an $ABX_3$ system)(1H) $J_{1',1'}$= 9Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 4.33(m)(1H) $J_{1,8}$≈ $J_{1,12}$≈ $J_{1,12}$≈ 3Hz C-H(1); 4,69(dd)(1H) $J_{4,5}$= 3.3Hz, $J_{4,9}$≈ 1Hz C-H(4). **$^{13}$C-NMR($CDCl_3$)(δ):** 15.6 C-2'; 16.7 C-11; 21.5 C-10; 26.8 C-12; 32.1 C-9; 39.5 C-8; 49.1 C-5; 49.6 O<u>C</u>$H_3$; 50.8 O<u>C</u>$H_3$; 52.4 C-7; 59.0 C-1'; 65.4 C-4; 75.2 C-1; 108.4 and 110.0 C-3 and C-6. **MS:** 304($M^+$)(3%), 302($M^+$)(8%), 272($M^+$-$CH_2O$), 267($M^+$-Cl)(100%), 163(92%), 161(24%), 157(32%), 121(26%), 115(28%), 101(28%), 91(25%), 88(56%).

**(±)-Bicyclo[4.3.0]nona-1',6'-dien-8'-on-7'-yl acetic acid (23) and Methyl bicyclo[4.3.0]nona-1',6'-dien-8'-on-7'-yl acetate (24):** **22** (117mg) in dioxane (3.7ml) and dil. hydrochloric acid (0.6ml; 2%)

were heated in a sealed tube (140°C; 1d). After evaporation of the solvent a crystalline substance resulted (**23**: UV: $\lambda_{max}$(ethanol)= 285nm). Since this unstable acid was difficult to separate from impurities it was treated with an excess of ethereal diazomethane. The resulting methyl ester **24** was chromatographed with petroleum ether : diethyl ether (3:1) yielding purified **24** (21.8mg; 47%).

**24**: **IR ($CCl_4$)($cm^{-1}$):** 3035, 3002, 1748, 1708, 1623. **$^1$H-NMR($CDCl_3$)(δ):** 1.84(quint)(2H) $J_{4',5'}$= $J_{4',5'}$= $J_{3',4'}$= $J_{3',4'}$= 6.5Hz C-H(4'); 2.31(dt)(2H) $J_{2',3'}$= 4Hz, $J_{3',4'}$= $J_{3',4'}$= 6.5Hz C-H(3'); 2.63(t)(2H) $J_{5',4'}$= $J_{5',4'}$= 6.5Hz C'-H(5'), 2.95(s)(2H) C-H(9'); 3.30(s)(2H) C-H(2); 3.69(s)(3H) OC-$H_3$; 6.03(t) $J_{2',3'}$= $J_{2',3'}$= 4Hz C-H(2'). **$^{13}$C-NMR($CDCl_3$)(δ):** 21.9 C-4'; 24.8 C-3'; 25.3 C-5'; 28.3 C-2; 38.1 C-9'; 52.1 O<u>C</u>$H_3$; 126.3 C-2'; 131.8 C-1'; 135.2 C-7'; 166.8 C-6'; 170.7 C-1; 204.1 C-8'. **MS:** 206($M^+$)(64%), 175($M^+$-$CH_3O$)(17%), 174($M^+$-$CH_3OH$)(32%), 147($M^+$-$COOCH_3$)(49%), 146($M^+$-$HCOOCH_3$)(100%), 91(44%).

**(±)-(1S*,3R*,5R*,6R*,7S*,8S*,9R*)-3-Ethoxy-6-methyl-2-oxatetracyclo[6.4.0.0$^{3,7}$.0$^{5,9}$]dodecan-6-ol (26)** and **(±)-(1S*,3R*,5R*,6S*,7S*,8S*,9R*)-3-ethoxy-6-methyl-2-oxatetracyclo [6.4.0.0$^{3,7}$.0$^{5,9}$]dodecan-6-ol (27):** To a solution of methyl magnesium iodide(5.5mmol) in diethyl ether(abs.; 2.5ml) was added **25** (0.6g; 2.7mmol) dissolved in diethyl ether(abs.; 5ml), and the resulting solution refluxed for 1 h. The cooled reaction mixture was treated with aqu. sat. $NH_4Cl$ and four times extracted with dichloromethane. The org. layers were washed with brine, dried over $MgSO_4$, filtered and the solvent evaporated. Flash chromatography on silica gel with petroleum ether : acetone (9:1) yielded **26** (0.226g; 35%) and **27** (0.305g; 47.5%).

**26 : IR($CCl_4$)($cm^{-1}$):** 3570,3600-3200small. **$^1$H-NMR($CDCl_3$)(δ):** 1.23(t)(3H) $J_{1',2'}$= 7.2Hz C-H(2'); 1.36(s)(3H) C(6)C-$H_3$; 1.24-1.42(m)(2H) C-H(12exo),C-H(11endo); 1.6-1.9(m)(5H) C-H(10exo), C-H(10endo), C-H(11exo), C-H(5), C-H(12endo); 2.16( part A of an ABX system)(1H) $J_{4,4}$= 14Hz, $J_{4,5}$= 0 C-H(4endo); 2.27(part B of an ABX system)(1H) $J_{4,4}$= 14Hz, $J_{4,5}$= 4Hz C-H(4exo); 2.21-2.36(m)(4H) C-H(8), C-H(9), C-H(7), O-H; 3.6(part A of an $ABX_3$ system)(1H) $J_{1',1'}$= 9Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 3.76(part B of an $ABX_3$ system)(1H) $J_{1',1'}$= 9Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 4.29(m)(1H)$w_{1/2}$= 9Hz C-H(1). **$^{13}$C-NMR($CDCl_3$)(δ):** 15.7 C-2'; 16.9 C-11; 20.9 C(6)-<u>C</u>$H_3$; 23.6 C-10; 27.5 C-12; 31.8 C-9; 38.5 C-5; 39.0 C-4; 49.7 C-8; 56.3 C-7; 58.9 C-1'; 73.6 C-1; 82.4 C-6; 115.6 C-3. **MS:** 238($M^+$)(10%), 223($M^+$-$CH_3$)(4%), 220($M^+$-$H_2O$)(8%), 177(25%), 147(41%), 131(38%), 115(100%), 107(26%), 93(32%), 91(19%), 43(87%).

**27 : IR($CCl_4$)($cm^{-1}$):** 3620, 3480br. **$^1$H-NMR($CDCl_3$)(δ):** 1.22(t)(3H) $J_{1',2'}$= 7.2 C-H(2'); 1.28-1.44(m)(2H) C-H(12exo), C-H(11endo); 1.44(s)(3H) C(6)C-$H_3$; 1.6-1.8 (m)(5H) C-H(10endo), C-H(5), C-H(10exo), C-H(11exo) and O-H; 1.89(m)(1H) $J_{12,12}$= 13Hz; $J_{12,11endo}$= $J_{12,11exo}$= $J_{12,1}$= 3-4Hz C-H(12endo); 1.94( part A of an ABXY system)(1H) $J_{4,4}$= 13Hz, $J_{4,5}$= 3.5Hz, $J_{4,9}$= 2Hz C-H(4exo); 2.07( part B of an ABXY system) $J_{4,4}$= 13Hz, $J_{4,5}$= $J_{4,9}$= 0Hz C-H(4endo); 2.37(m)(1H) $J_{7,8}$= 5Hz, $J_{7,5}$= 1.5Hz C-H(7); 2.48(m)(1H) $J_{8,9}$= 10Hz, $J_{8,1}$= $J_{8,7}$= 5Hz C-H(8); 2.73(m)(1H) $w_{1/2}$= 20Hz C-H(9); 3.54(part A of an $ABX_3$ system)(1H) $J_{1',1'}$= 9,5Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 3.69(part B of an $ABX_3$ system)(1H) $J_{1',1'}$= 9,5Hz, $J_{1',2'}$= 7.2Hz C-H(1'); 4.26(m)(1H) $w_{1/2}$= 10Hz C-H(1). **$^{13}$C-NMR($CDCl_3$)(δ):** 15.6 C-2'; 17.1 C-11; 20.8 C(6)-<u>C</u>$H_3$; 23.3 C-10; 27.7 C-12; 31.8 C-9; 39.3 C-4; 40.2 C-5; 49.5 C-8; 56.5 C-7; 58.6 C-1'; 73.1 C-1; 81.6 C-6; 113.4 C-3. **MS:** 238($M^+$)(12%), 223($M^+$-$CH_3$)(10%), 220($M^+$-$H_2O$)(17%); 177(36%), 147(66%), 132(34%), 131(33%), 115(87%), 107(24%), 105(26%), 93(37%), 91(21%), 43(100%).

**(±)-(1R*,2R*,6R*,7S*)-2-Acetyl-7-hydroxybicyclo[4.4.0]decan-4-one (28) and (±)-(1R*,2S*,6R*,7S*)-2-Acetyl-7-hydroxybicyclo[4.4.0]decan-4-one (29):**

a) Starting from alcohol **27**: To a solution of **27** (80mg; 0.34mmol) in dry acetonitrile (6ml) at 0°C was

added $BF_3$.$OEt_2$ (0.5ml) and the mixture was stirred for 5 h. Then sat. aqu. $NaHCO_3$ was added and the mixture was extracted with dichloromethane. The org. layers were washed with brine, dried over $MgSO_4$, and the solvent evaporated. Flash chromatography on silica gel with diethyl ether : petroleum ether : ethyl acetate (6:1:1) yielded **28** (51mg; 72%).

**b)** Starting from alcohol **26**: To a solution of **26** (80mg; 0.34mmol) in dry acetonitrile (6ml) at room temperature was added $BF_3$.$OEt_2$ (0.5ml) and the mixture was stirred for 5 h. Then sat. aqu. $NaHCO_3$ was added and the mixture was extracted with dichloromethane. The org. layers were washed with brine, dried over $MgSO_4$, and the solvent evaporated. Flash chromatography on silica gel with diethyl ether : petroleum ether : ethyl acetate (6:1:1) yielded **28** (37mg; 52%) along with its stereoisomer **29** (16mg; 23%).

**28**: **IR($CCl_4$)(cm$^{-1}$):** 3620, 3420 br., 1715. **$^1$H-NMR($CDCl_3$)(δ):** 1.4-1.7(m)(5H) C-H(8), C-H(9), C-H(10); 1.84(m)(1H) C-H(9); 2.11(s)(1H) O-H; 2.22(s)(3H) C-H(2'); 2.2-2.6(m)(6H) C-H(1), C-H(3), C-H(5), C-H(6); 3.43(m)(1H) $J_{1,2}\approx J_{2,3exo}\approx J_{2,3endo}\approx$ 6Hz C-H(2); 3.92(m)(1H) $J_{6,7}\approx J_{7,8exo}\approx J_{7,8endo}\approx$ 4Hz C-H(7). **$^{13}$C-NMR($CDCl_3$)(δ):** 20.0 and 26.9 C-9 and C-10; 29.4 C-2'; 30.5 C-8; 35.4 C-1; 39.8 and 40.0 C-3 and C-5; 40.4 C-6; 52.4 C-2; 71.0 C-7; 210.2 and 210.5 C-1' and C-4. **MS:** 210($M^+$)(2.2%), 192($M^+$-$H_2O$)(19%), 167($M^+$-$CH_3CO$)(3%), 149($M^+$-$H_2O$-$CH_3CO$)(14%), 121($M^+$-$H_2O$-$CH_3CO$-CO)(12%), 107($M^+$-$H_2O$-$CH_3CO$-$CH_2CO$)(26%), 43($CH_3CO^+$)(100%).

**29**: **IR($CCl_4$)(cm$^{-1}$):** 3620, 3420 br., 1715. **$^1$H-NMR($CDCl_3$)(δ):** 1.04(m)(1H) C-H(9exo); 1.31(m)(3H) C-H(8endo), C-H(10exo), C-H(10endo); 1.63(m)(1H) C-H(8exo); 1.76(m)(1H) C-H(9endo); 2.10(s)(3H) C-H(2'); 2.0-2.4(m)(6H) C-H(1), C-H(3exo), C-H(5exo), C-H(5endo), C-H(6), O-H; 2.59(m)(1H) $J_{2,3endo}$= 14Hz, $J_{3exo,3endo}$= 14Hz C-H(3endo); 2.89(m)(1H) $J_{1,2}$= 4Hz, $J_{2,3exo}$= 4Hz, $J_{2,3endo}$= 14Hz C-H(2); 3.76(m)(1H) $J_{6,7}$= 3.6Hz, $J_{7,8exo}$= 3.6Hz, $J_{7,8endo}$= 10.2Hz C-H(7). **$^{13}$C-NMR($CDCl_3$)(δ):** 19.6 C-9 ; 23.1 C-10; 27.7 C-8; 28.0 C-2'; 35.3 and 38.1 C-3 and C-5; 36.5 C-1; 43.6 C-6; 53.9 C-2; 70.7 C-7; 207.4 and 211.9 C-1' and C-4. **MS:** 210($M^+$)(2.5%), 192($M^+$-$H_2O$)(7.8%), 167($M^+$-$CH_3CO$)(2.4%), 149($M^+$-$H_2O$-$CH_3CO$)(7.2%), 121($M^+$-$H_2O$-$CH_3CO$-CO)(7.8%), 107($M^+$-$H_2O$-$CH_3CO$-$CH_2CO$)(21%), 43($CH_3CO^+$)(100%).

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