SYNTHESES IN THE ISOCAMPHANE SERIES. XXXI[1]. 7-OXACAMPHENILONE, 7-OXACAMPHENE AND 7-OXACAMPHENILANIC ACID

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Abstract - The syntheses of the title compounds and their organoleptic properties are described. 7-Oxacamphenilone (2) has been obtained by two-fold methylation of 7-oxanorbornan-2-one (1). The synthesis of 7-oxacamphene (5) has been accomplished by dehydration of 7-oxamethylcamphenilol (4). 7-Oxacamphenilanic acid (8) and some derivatives have been prepared starting with 5 by means of a hydroboration step and subsequent oxidation.

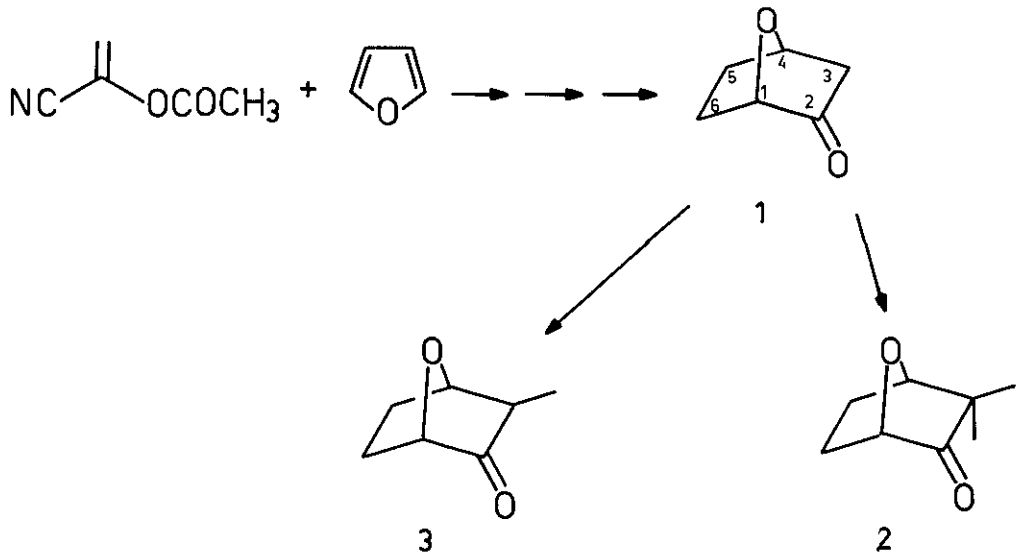
INTRODUCTION

In continuation of our syntheses of isocamphane analogous drugs[1] and bicyclic fragrance compounds[3,4,5] we took an interest in changing the bridge-CH_2-group of the norbornane skeleton into an ether bridge, thus preparing 7-oxa-bicyclo[2.2.1]-heptane derivatives with the aim to study the dependence of their biological (mainly organoleptic) properties on structure modifications. In this paper therefore we want to report upon the synthesis of the title compounds and of some other 7-oxanorbornanes.

RESULTS

The construction of the 7-oxanorbornane skeleton via Diels-Alder reaction in most cases proves to be very tedious because of the poor reactivity of furan in a [4+2]-cycloaddition. These difficulties we encountered during our efforts to add mesityl oxide or senecioic acid derivatives (e.g. nitrile) or even the less sterically crowded crotonic acid derivatives (e.g. nitrile, aldehyde) to furan. Neither heating the reaction mixture, nor applying higher pressure (approximatively 100 bar), nor Lewis-acid catalysis, nor longer reaction times led to the corresponding

7-oxanorbornane derivative.But we succeeded to synthesize the title compound 7-oxacamphenilone (2)* via 7-oxanorbornane-2-one (1) which itself could be obtained by a Diels-Alder reaction of furan with the ketene equivalent acetoxyacrylonitrile according to the method of Vogel[6,7] and Brion[8]. Twofold methylation of 1 with methyl iodide/potassium tert.-butoxide in THF[9] directly led to 2, whereas 7-oxaapocamphenilone (3), the monomethyl derivative, is available by conventional methylation of 1 with one equivalent methyl iodide and LDA. The camphenilone analogue 2 could also be obtained from 3** by a second methylation step, but the purification of the resulting reaction mixture consisting of 80% 2 and of 20% not completely converted 3 (as shown by capillary GC) by flash chromatography proved to be tedious.



* In part already reported at the 10th International Congress of Essential Oils in Washington D.C., November 18,1986.

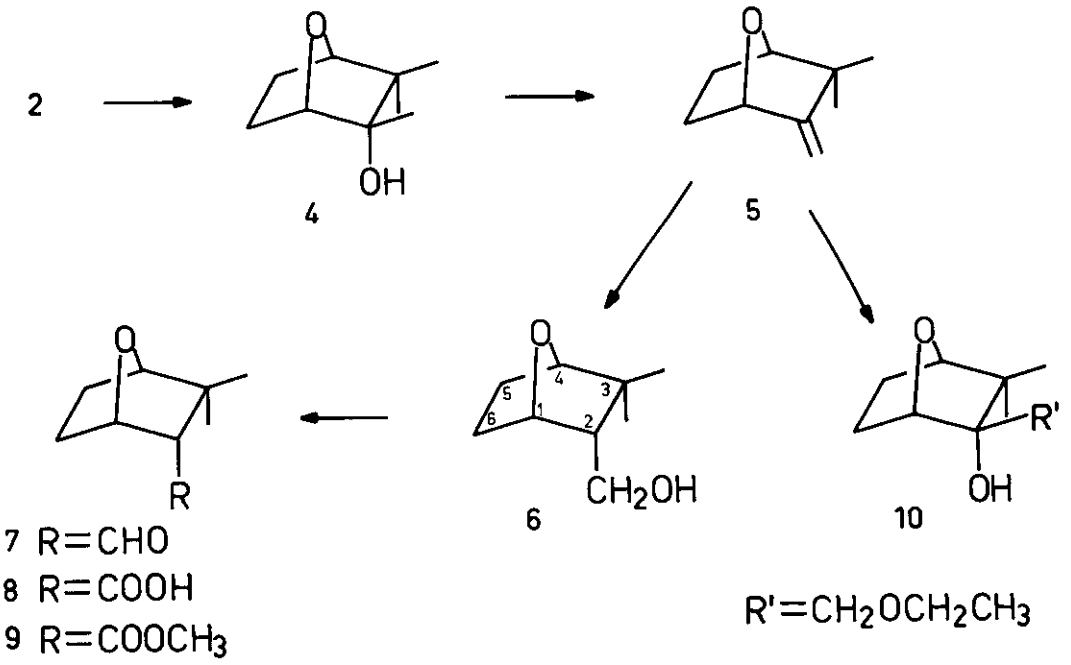
** After delivering our manuscript for the 10th International Congress of Essential Oils (deadline: June 1,1986) also Warm and Vogel[10] reported upon the synthesis of 3 by a somewhat different method and presenting one argument in favour of the exo-methyl group.

Two routes to **1** had also been tried in order to avoid the sumptuous preparation of the starting dienophile acetoxyacrylonitrile, but failed already in the first step: [4+2]-cycloaddition of furan to vinylic acetate or to vinylmethyl ketone according to the method of Laszlo et al.[11]

The position of the single methyl group in **3** has been elucidated by means of ^{1}H-NMR-spectroscopy as follows: The two bridgehead protons C_1-H and C_4-H in the nor-methyl product **1** could be found at 4.44 ppm (C_1-H) as a doublet and at 4.92 ppm (C_4-H) as a multiplet. The spin multiplicity of these signals is characteristic, because the C_1-H is able to couple only with the C_8-H$_{exo}$ and not with the C_8-H$_{endo}$ proton. In this case the dihedral angle between C_1-H and C_8-H$_{endo}$ is approximatively 90°, as could be found out after measuring a Dreiding-model. On the other hand the C_4-H can couple with both exo-configurated protons at C_3 and C_5 thus forming the observed multiplet. If one of these two carbon atoms bears a methyl group in the exo-position as in compound **3** the C_4-H lacks a coupling partner. Thus the C_4-H in **3** appeared as a doublet at 4.36 ppm. (If the methyl group would be in the endo-position, one should observe the signal of the C_4-H as a multiplet). In addition to these results we are able to present another proof of the exo-position of the methyl group in **3**. The endo-proton at C_3 does not couple with the C_4-H as we have shown above but couples with the methyl group protons forming a quartet. In **3** this quartet is hidden under a lot of signals in the upfield region but in the dinitrophenylhydrazone of **3** it is shifted downfield to 2.64 ppm where this C_3-H$_{endo}$ could be detected as a neat quartet without any other coupling. Finally we are able to present a last proof of the exo-position of the methyl group in **3** based upon data of the ^{13}C-NMR-spectrum. The difference of the chemical shifts of C_5 in the structures **3** and **1** where the methyl group assumes the exo-position compared with the corresponding carbon atom in the nor-derivative **1** is negligible, whereas the new additional methyl group in **2** causes a 3ppm upfield shift of the signal of C_5 by means of a γ-gauche-effect[12], thus proving its endo-position and therefore the exo-position of the first methyl substituent.

The next synthetic goal has been realized by the synthesis of 7-oxacamphene (**5**) via 7-oxamethylcamphenilol (**4**) starting with **2**. We obtained the tertiary alcohol **4** upon reaction of **2** with methyl lithium as a single product in nearly quantitative yield. The right position of the hydroxyl group has been determined by NOE-experiments: irradiation upon the new methyl group at C_2 caused an NOE upon both methyl groups at C_3 but none upon the endo-protons of C_5 and C_8 thus proving the exo-position of the newly introduced methyl group and the endo-position of the hydroxy function. Finally we are able to present another proof of the structure **4** as follows: the relative intensities of the signals of the C_5- and C_8-protons are 1:1:2 and not 2:2, thus showing a different shielding effect upon C_5-H$_{endo}$ and C_8-H$_{endo}$ caused by the endo-hydroxyl group at C_2. The dehydration of the tertiary alcohol **4** to 7-oxacamphene (**5**) by means of $POCl_3$/pyridine succeeded with good yields. The spectroscopic data are in accordance to the postulated structure.

The camphene analogue **5** now served as starting material for the construction of the C_1-side chain of 7-oxacamphenilanic acid (**8**) and its derivatives. Hydroboration of **5** by means of 9-BBN led to a 97·3 mixture of endo-**6**:exo-**6** which could be purified by flash chromatography (chloroform: ethyl acetate = 85:15).



The proof of the existence of the pure endo-compound **6** has been offered again by the ^{1}H-NMR-spectrum: C_1-H is able to couple with C_6-Hexo and C_2-Hexo, whereas C_4-H lacks the second possibility and couples only with C_5-Hexo. Thus the different shape of the two signals of C_1-H and C_4-H as well as the relative intensities of the signals of the C_5- and C_6-protons as 1:1:2 is characteristic for the endo-position of the substituent at C_2. Oxidation of **6** by means of 2,2'-bipyridyl chlorochromate led to the aldehyde **7**, which is very prone for an autooxidation to its corresponding acid **8** , also obtainable by direct oxidation of **6** with $KMnO_4$. 7-Oxacamphenilanic acid methyl ester (**9**) could be prepared by action of diazomethane upon **8**. In all cases the endo-position of the substituent at C_2 is retained.

We also tried another possibility to build up the C1-side chain of the 7-oxa-camphenilanic system. Nearly twenty years ago Botton[13] obtained isocamphenilanic acid by a Grignard reaction of camphenilone and chloromethyl ethyl ether, subsequent ether cleavage to isocamphenilanic aldehyde and finally oxidation of this intermediate to the corresponding acid. We repeated this reaction sequence starting with **2** which could be transformed into the hydroxy ether **10** with excellent yields. But contrary to the findings of Botton we were not able to cleave the ether **10** even under more rigorous reaction conditions, which resulted only in destroying the molecule. Also experiments to create the corresponding enol ether by dehydration of **10** were in vain.

The organoleptic properties of the new compounds **1** - **10** have been evaluated. According to the theory of Amoore[14] one could expect a camphoraceous odour because of the spherical shape of the molecules. But **1** lacks this odour completely (**1** smells mainly fruity, ethereal, a bit flowery and somewhat reminiscent to THF) and the fruity smelling **3** only shows some traces of a camphoraceous note. But a clear and strong camphoraceous odour possesses the camphenilone analogue **2** and **4** shows a strong earthy, cellarlike and musty odour. The odour of 7-oxacamphene (**5**) has been defined as smooth camphoraceous, with a note of eucalyptus and rosemary, somewhat reminiscent to camphor oil. Finally the compounds **6** - **10** have a weak camphorlike-dull-musty odour.

EXPERIMENTAL

General remarks, equipment, conditions: see lit.[15]. IR-spectra: Perkin Elmer 298 Infrared Spectrophotometer (NaCl, liquid film, band values in cm^{-1}). GC: Varian 3700, SE 52 fused silica. Flash chromatography: Silica gel 60 (Merck-number9385), pressure: $0.7.10^5$ Pa nitrogene. NMR-spectra: δ-values in ppm; TMS inner standard.

7-Oxa-bicyclo[2.2.1]heptan-2-one (1)

According to lit.[16] **1** has been prepared in three steps: a) Diels-Alder reaction of 25 g (225 mmol) of acetoxyacrylonitrile, 21.8 g (67 mmol) of ZnI_2 and 30 g (450 mmol) of furan, yield 55%; b) hydrogenation of the adduct, yield 96 %; c) saponification and oxidation of the hydrogenated adduct, yield 11.23 g (85%) of **1**.

Oxime: colourless, very viscious oil; bp 145°C/0.5mm. IR: 3300.
^{1}H-NMR ($CDCl_3$): 1.38-2.41(m,4H,C5-H and C8-H); 2.57(dd,J=4.5Hz,J=16.5Hz,2H,C3-H); 4.6-4.95(m,2H,C1-H,C4-H); 8.0-8.52(br, 1H, OH). MS(m/z;r.i.): 127(M^+,22); 110(100), 98(22); 82(31); 80(15); 70(16); 55(61); 53(29); 41(63).

3-exo-Methyl-7-oxa-bicyclo[2.2.1]heptan-2-one (7-oxaapocamphenilone) (3)

To a stirred solution of lithium diisopropylamide (LDA, 14.7 mmol) in 30 ml of dry THF under argon at -78°C 1.5g (13.4 mmol) of 1 was added dropwise. After 2 h, 1ml (16.1 mmol) of CH_3I was added dropwise at the same temperature and the resulting mixture was warmed up to room temperature overnight. After quenching with one equivalent of saturated aqueous NH_4Cl-solution the THF was distilled off and the resulting residue was extracted thoroughly with ether. Then the combined ethereal extracts were washed with 2N HCl and water. After evaporation of the solvent in vacuo the residue was steam distilled, the distillates were extracted with $CHCl_3$ and the organic layers were dried over sodium sulfate and finally concentrated in vacuo. The resulting residue was distilled in a kugelrohr apparatus to furnish 800 mg (47.4%) of a slightly yellow oil,bp 65-67°C/0.5mm. $C_7H_{10}O_2$ (126.16). ^{1}H-NMR ($CDCl_3$): 1.20 (d,J=7 Hz,3H,CH_3); 1.64-1.77 (m,2H,C_5-Hendo and C_6-Hendo); 1.89-2.09 (m, 3H, C_3-Hendo; C_5-Hexo and C_6-Hexo); 4.36 (d,1H, C_4-H); 4.47 (d,1H, C_1-H). ^{13}C-NMR ($CDCl_3$): 215.2 C_2; 81.75 C_1; 79.6 C_4; 48.44 C_3; 27.99 C_6; 24.19 C_5; 13.97 C_7. MS(m/z;r.i.): 126(M^+,18); 111(24); 98(43); 83(31); 80(12); 70(28); 69(77); 56(27); 55(73); 42(60); 40(100). 2,4-dinitrophenylhydrazone: Orange-yellow needles (alcohol),mp 176°C. Anal. calcd for $C_{13}H_{14}N_4O_5$ C,50.98; H,4.60; N,18.30. Found: C,50.44; H,4.50; N,18.50. ^{1}H-NMR ($CDCl_3$): 1.40 (d,J=7 Hz,3H, C_3-CH_3); 1.54-1.80 (m,2H,C_5-Hendo,C_6-Hendo); 1.85-2.11 (m,2H,C_5-Hexo,C_6-Hexo); 2.64 (qu,1H,C_3-Hendo); 4.46 (m, 1H,C_4-H);4.92 (m,1H,C_1-H); 7.86 (d,J=10 Hz, 1H, C_6-H); 8.3 (dd, J=3.2 Hz, J= 10 Hz, 1H, C_5-H) 9.11 (d, J=3.2 Hz, 1H, C_3-H); 10.91 (1H, N-H). MS(m/z;r.i.): 306(M^+,50); 277(13); 270(17); 124(13); 111(20); 109(13); 98(57); 81(88); 69(70); 55(55); 41(100).

3,3-Dimethyl-7-oxabicyclo[2.2.1]heptan-2-one (7-oxacamphenilone) (2)

a) To a stirred solution of LDA (5.8 mmol) in 30ml of dry THF under argon at -78°C 0.66 g (5.23 mmol) of 3 was added dropwise. After 2 h, 1ml of CH_3I was dropped to the reaction mixture and the whole suspension was warmed to room temperature overnight. Then the reaction was quenched with 1 equivalent of aqueous NH_4Cl-solution, THF was distilled off and the resulting residue was extracted with ether. The combined organic layers were washed with 2N HCl at first, then with brine and finally dried over sodium sulfate. After evaporation of the solvent the residue was steam distilled. The distillates were extracted thoroughly with $CHCl_3$ and the combined organic layers were dried over sodium sulfate and then set free from the solvent by evaporation. The residue was distilled in the kugelrohr to furnish a slightly yellow oil in 40-60% yield.

b) To a stirred solution of 2g (17.8 mmol) of 1 and 1.5 ml (24 mmol) of CH_3I in 20 ml of dry THF under argon at 0°C was added dropwise a solution of 2.1g (18.7 mmol) potassium tert.-butoxide in 20 ml of dry THF. After 30 min the cooling bath was taken away and the reaction mixture was stirred at room temperature for 2 h. Then 3.8 g (26.7 mmol) of CH_3I and 2 g (17.8 mmol) of potassium tert.-butoxide in 20 ml of dry THF were added again at 0°C. After 30 min at 0°C and 2 h at room temperature

the reaction was quenched with saturated aqueous NH_4Cl-solution. Further work up as before and kugelrohr distillation furnished 2.25 g (90%) of a slightly yellow oil, bp 70-72°C/0.5 mm. IR: 1760, 1460, 1390 and 1365, 1070. ^{1}H-NMR ($CDCl_3$): 1.02 (s,3H, CH_3-endo); 1.22 (s,3H,CH_3-exo); 1.54-2.05 (m,4H,C_5-H and C_6-H); 4.34 -4.43 (m, 2H, C_1-H and C_4-H). ^{13}C-NMR($CDCl_3$): 220.3 C_2, 89.19 C_1, 80.37 C_4, 48.94 C_3, 25.28 C_8, 23.70 C_5, 22.82 C_8, 19.80 C_7. MS (m/z; r.i.): 140 (M^+,21); 112(22); 97(26); 94(33); 79(22); 71(17); 69(53); 56(100); 55(34); 41(82).

2-exo,3,3-Trimethyl-7-oxa-bicyclo[2.2.1]heptan-2-ol (7-oxamethylcamphenilol) (**4**)

To a vigorously agitated solution of CH_3Li (8 mmol) in 10 ml of dry diethyl ether 0.7 g (5 mmol) of **2** was added dropwise and the resulting mixture was stirred at room temperature for 90 h. After hydrolyzing with saturated aqueous NH_4Cl-solution (completely resolving of the precipitate is necessary) the organic layer was separated and the aqueous layer was extracted with ether several times. The combined ethereal extracts were washed with brine, dried over sodium sulfate and freed from the solvent. Kugelrohr distillation of the residue furnished 0.63 g (81%) of **4** as a colourless oil, bp 77-79°C/ 0.5 mm, IR:3450, 1460, 1390 and 1365, 1070. ^{1}H-NMR ($CDCl_3$): 0.92 (s,3H,CH_3-endo); 1.05 (s, 3H, CH_3-exo); 1.3 (s, 3H, C_2-CH_3-exo); 1.5 (m,2H, C_5-H$_{exo}$ and C_8-H$_{exo}$); 1.6-1.79 (br, 1H, OH); 1.77-1.97 (m,1H, C_5-H$_{endo}$); 2.08-2.28 (m,1H,C_8-H$_{endo}$); 3.95 (m,1H,C_4); 4.04 (m,1H,C_1-H). ^{13}C-NMR ($CDCl_3$): 88.60 C_1; 86.87 C_4; 78.38 C_2; 44.63 C_3; 26.15 C_8; 25.43 C_5; 24.68 C_9; 22.72 C_7; 20.23 C_8. MS (m/z; r.i.): 156 (M^+,4); 141(13); 113(18); 99(48); 95(26); 85(15); 83(18); 74(14); 71(26); 70(24); 69(29); 55(14); 43(100); 41(37).

3,3-Dimethyl-2-methylen-7-oxa-bicyclo[2.2.1]heptane (7-oxacamphene) (**5**)

To a stirred solution of 3.4 g (21.8 mmol) of **4** in 30 ml of dry pyridine under argon at 0°C 5.6ml (61.2 mmol) of $POCl_3$ was added dropwise and the mixture was warmed up to room temperature and stirred for 12 h. After hydrolyzing with ice water the mixture was extracted with ether. The combined ether layers were washed with 2N HCl , then with aqueous $NaHCO_3$-solution and finally with a saturated aqueous $CuSO_4$-solution to remove a trace of pyridine. After drying over sodium sulfate the solvent was distilled off and the oily residue was purified by flash chromatography with $CHCl_3$ as eluent to give 1.45 g (48%) of **5** as a colourless oil. Bp 42° C/0.5 mm, IR: 3060, 1670, 1460, 1390 and 1360, 1070. ^{1}H-NMR ($CDCl_3$): 1.08 (s, 3H, CH_3-endo); 1.15 (s, 3H, CH_3-exo); 1.49-1.68 (m,2H, C_5-H$_{endo}$ and C_8-H$_{endo}$); 1.74 - 1.92 (m,2H,C_5-H$_{exo}$ and C_8-H$_{exo}$); 4.09 (m,1H,C_1-H); 4.60 (m,1H,C=C-H); 4.73 (m,1H, C_4-H); 4.80 (m, 1H, C=C-H). ^{13}C-NMR ($CDCl_3$): 162.04 C_7; 99.5 C_2;86.03 C_4; 81.81 C_1; 45.32 C_3; 30.28 C_6; 28.82 C_8; 24.28 C_5; 23.55 C_9. MS (m/z; r.i.): 138 (M^+,28); 123(25); 110(27); 109(43); 95(65); 81(37); 79(56); 69(49); 55(38); 41(100); 39(62).

3,3-Dimethyl-7-oxa-bicyclo[2.2.1]heptan-2-endo-methanol (7-oxacamphenilanol) (6)

According to the method of Brown[17] 1.7 g (12.3 mmol) of 5 was added slowly under argon to a stirred solution of 1.5 g (12.3 mmol) of 9-BBN in 25 ml of dry THF. After stirring for 4 h the reaction mixture was oxidized by addition of a mixture of 7.4 ml of ethanol, 2.5 ml of 6N aqueous NaOH and 5 ml of 30 % H_2O_2 and then stirred at 50°C for 1 h. After cooling to room temperature the solution was saturated with K_2CO_3, and the organic layer was separated. The aqueous layers were extracted twice with ether. The combined organic layers were dried over sodium sulfate and concentrated in vacuo. The crude oily residue was purified by flash chromatography ($CHCl_3$: ethyl acetate = 85:15). Yield: 1.2 g (62.5 %) of **6** as a colourless oil (bp 64°C/0,5 mm), IR: 3400. ^{1}H-NMR ($CDCl_3$): 0.89(s, 3H, CH_3-endo; 1.09 (s, 3H, CH_3exo); 1.49-1.93 (m,5H, C_2-Hexo, both C_5- and C_8-H); 2.74 (s,1H, OH); 3.50 (dd,J=9Hz, J=10Hz, 1H, C_8-H); 3.65 (dd, J=6.5 Hz, J=10 Hz, 1H, C_8-H); 3.93 (m,1H, C_4-H); 4.54 (m, 1H,C_1-H). ^{13}C-NMR ($CDCl_3$): 86.79 C_1; 80.18 C_4; 60.7 C_8; 53.53 C_2; 40.39 C_3; 31.95 C_9; 24.84 C_6; 22.71 C_5; 18.8 C_7. MS (m/z; r.i.): 87 (M+-70;10); 85(65); 83(100); 48(21); 47(47); 43(59).

3,3-Dimethyl-7-oxa-bicyclo[2.2.1]heptan-2-endo-carbaldehyde (7-oxacamphenilane-aldehyde) (7)

Compound **6** (0.45g, 2.9 mmol) was oxidized with 2.53 g (8.7 mmol) of 2,2'-bipyridyl-chlorochromate according to the procedure of Guziec et al.[18] After 4 h the reaction mixture was diluted with dry diethyl ether and decanted from the black residue. Then the organic layer was filtered through a pad of silica gel and celite 545 and the filtrate was washed with 5% HCl and a 10% aqueous $NaHCO_3$-solution and dried over sodium sulfate. After evaporation of the solvent there remained 200 mg (45 % yield) of **7** as a slightly yellow oil, bp 53°C/0.5 mm. ^{1}H-NMR ($CDCl_3$): 1.16 and 1.22 (2s, 6H,CH_3-endo and CH_3-exo); 1.42-2.49 (m,5H, C_2-H and both C_5- and C_8-H); 3.91-4.13 (m, 1H, C_4-H); 4.54-4.75 (m, 1H, C_1-H); 9.75 (m, 1H).

3,3-Dimethyl-7-oxa-bicyclo[2.2.1]heptan-2-endo-carboxylic acid (7-oxacamphenilanic acid) (8)

Compound **7** (500 mg, 3.2 mmol) was stirred in a solution of 86 mg of KOH in 20 ml of H_2O and $KMnO_4$ (850 mg, 5.38 mmol) was added within 6 h. After filtration the clear filtrate was mixed with methanol and again filtered, then acidified with HCl and extracted with ether. The combined organic layers were dried over sodium sulfate and concentrated in vacuo. The resulting residue after kugelrohr distillation gave 470 mg (86%) of **8** as white platelets, mp 78°C. IR: 3600 -

3100;,1725;,1460;,1390 and 1360. ^{1}H-NMR(CDCl$_3$): 1.09 and 1.25 (gem.CH$_3$); 1.47-1.76 (m,2H,C$_5$-Hexo and C$_6$-Hexo); 1.83 -1.96 (m,1H, C$_5$-Hendo); 2.22-2.34 (m, 1H, C$_6$-Hendo); 2.67 (d,1H, J=4.8 Hz, C$_2$-Hexo); 4.09 (m,1H, C$_4$-H); 4.65 (m,1H,C$_1$-H); 9-10.75 (br, 1H, COOH). ^{13}C-NMR (CDCl$_3$): 177.3 C$_7$; 87.2 C$_1$; 79.5 C$_4$; 57.2 C$_2$; 42.3 C$_3$; 31.4 C$_8$; 25.1 C$_6$; 23.96 C$_5$; 21.2 C$_7$. MS (m/z; r.i.): 155 (M$^+$-15, 8); 142(27); 127(19); 126(22); 114(91); 113(44); 109(19); 95(23); 83(30); 82(35); 81(36); 70(33); 69(30); 67(35); 55(58); 53(29); 43(57); 41(100); 39(76).

Methyl 3,3-dimethyl-7-oxa-bicyclo[2.2.1]heptan-2-endo-carboxylate (7-oxacamphenilanic acid methyl ester) (9)

Compound 8 (400 mg, 2.4 mmol) was esterified as usual by diazomethane in 15 ml ether. The crude ester was purified by bulb to bulb distillation (bp 65°C/0.5 mm). Yield: 380 mg (86 %) 9 as colourless oil. IR: 1750. ^{1}H-NMR (CDCl$_3$): 1.0 and 1.21 (2s, 6H, both CH$_3$); 1.52-1.70 (m,2H, C$_5$-Hexo and C$_6$-Hexo); 1.85-1.92 (m, 1H, C$_5$-Hendo); 2.21-2.30 (m, 1H, C$_6$-Hendo); 2.61 (d,J=4.8 Hz, C$_2$-H); 3.66(s,3H, COOCH$_3$); 4.03 (m,1H,C$_4$-H); 4.61 (m,1H, C$_1$-H). MS (m/z; r.i.): 169 (M$^+$-15, 9); 156(22); 153(17); 141(15); 128(43); 127(36); 109(18); 107(24); 96(20); 95(25); 83(33); 81 (32); 71(27); 69(30); 67(35); 55(70), 43(44), 41(100); 39(64).

3,3-Dimethyl-2-exo-ethoxymethyl-7-oxa-bicyclo[2.2.1]heptan-2-ol (10)

Compound 2 (3g, 21.4 mmol) was mixed with 42.2 mmol of the ethereal Grignard solution of chloromethyl ethyl ether, then hydrolyzed with aqueous NH$_4$Cl-solution and the whole suspension extracted several times with ether. The combined organic layers were washed with brine, then dried over sodium sulfate and concentrated in vacuo. The residue proved itself as pure 10. Yield: 3,6 g (85 %). Slightly yellow oil, bp 65°C/0.5 mm. ^{1}H-NMR (CDCl$_3$): 0.93 (s,3H, CH$_3$-endo); 1.06 (s,3H, CH$_3$-exo); 1.22 (t, 3H,C$_{10}$-CH$_3$); 1.46-1.55 (m,2H, C$_5$-Hexo and C$_6$-Hexo); 1.84-1.96 (m,1H, C$_5$-Hendo); 2.12-2.23 (m,1H, C$_6$-Hendo); 2.6 (br, 1H, OH); 3.42 (qu, 2H, J=6Hz, C$_{10}$-H); 3.53 (qu, 2H, J=7Hz, C$_9$-H); 3.9 (m, 1H, C$_4$-H); 4.27 (m,1H, C$_1$-H). ^{13}C-NMR (CDCl$_3$): 88.4 C$_1$; 82.72 C$_4$; 79.17 C$_2$; 75.74 C$_8$; 66.75 C$_{10}$; 44.47 C$_3$; 24.69 C$_6$; 24.29 C$_7$; 22.84 C$_5$; 20.34 C$_8$; 15.23 C$_{11}$. MS (m/z; r.i.): 200 (M$^+$ 3); 154(34); 141(18); 129(21); 123(15); 115(100); 111(22); 101(15); 97(58); 95(68); 87(81); 83(32); 70(60); 69(95); 59(61); 43(77); 41(86).

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