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New camphor derived chiral ligands for asymmetric synthesis

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Abstract

New enantiomerically pure 1,4-diols and 1,4-aminoalcohols have efficiently been prepared in one and two steps, respectively, from a commercially available camphor derived *exo* fused lactone. Using sterically hindered amines, an aldol addition of two lactone molecules was observed and the stereochemistry of the products was determined by X-ray crystallography.

1. Introduction

Enantiomerically pure aminoalcohols and diols based on the (+)-camphor skeleton have found widespread use as chiral additives and auxiliaries in asymmetric synthesis.[1] Since Noyori and co-workers demonstrated the high catalytic activity of (−)-3-*exo*-dimethylamino isoborneol **1** (Fig. 1) in the addition of diethylzinc to aldehydes,[2–5] ligands with 1,2-functionalities have been predominantly used.[6] Besides a few examples[7] demonstrating the use of γ-aminoalcohols **2**, **3**, the synthesis and utilization of (+)-camphor and (−)-menthone derived 1,4-aminoalcohols **4**, **5** as ligands for diethylzinc have recently been shown.[8,9] Examples for camphor derived 1,3-diols **6** have been described by Mellao and Vasconcellos.[10]

In this report we describe the use of the readily available *exo*-lactone **7**[11,12] as a practicable starting material for the synthesis of 1,4-diols **8** and δ-aminoalcohols **10**, which may serve as chiral auxiliaries and ligands in asymmetric synthesis (Scheme 1, Table 1).

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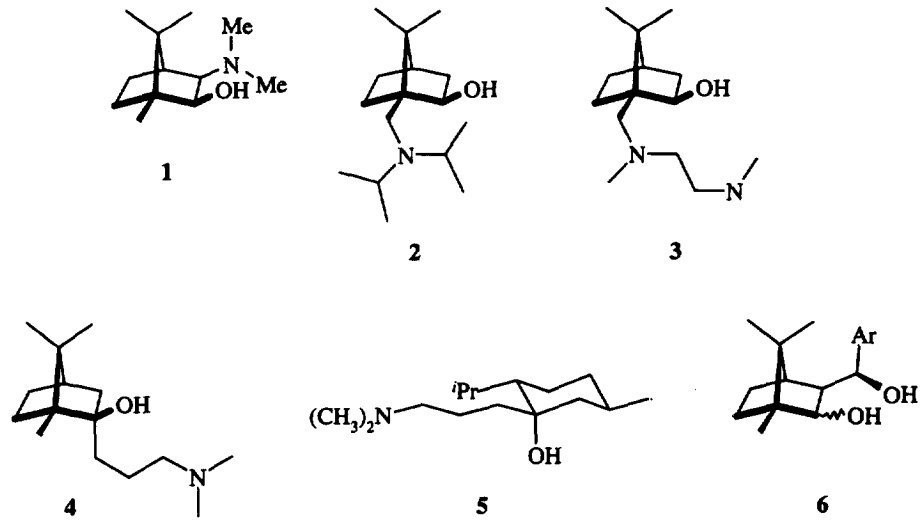
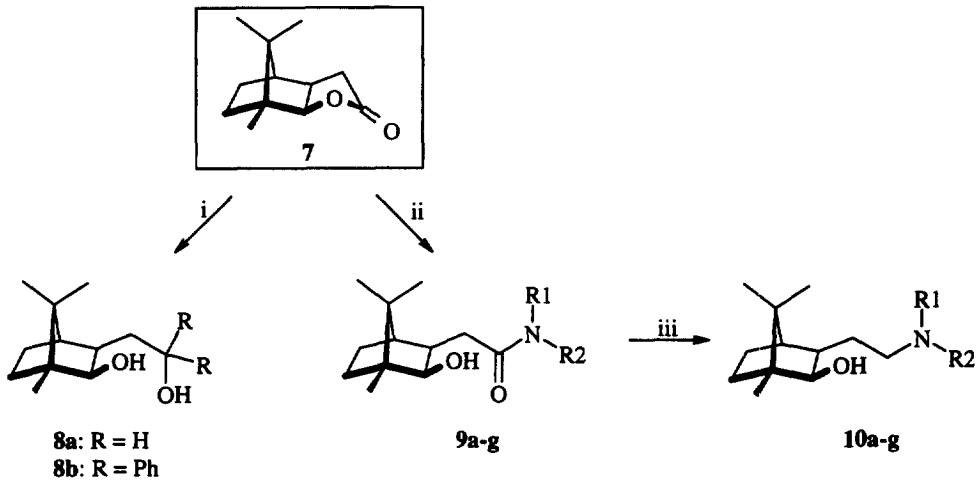


Figure 1. Examples of some aminoalcohols and diols as efficient ligands in asymmetric synthesis



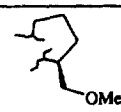
Scheme 1. (i) **8a**: $LiAlH_4$ in Et_2O, reflux for 1 h (99%); **8b**: PhLi in THF, r.t. for 7 h (75%); (ii) R1R2NH, $AlCl_3$ in 1,2-dichloroethane (12–97%); (iii) $LiAlH_4$ in Et_2O (82–98%)

2. Results and discussion

An obvious advantage in starting with **7** is the already well defined stereochemistry of the substituents in the 2- and 3-positions on the camphor skeleton. Thus, the 1,4-diol **8a** was obtained by simple reduction with lithium aluminum hydride and the reaction of **7** with phenyllithium afforded **8b**. The latter substance carries the diphenyl hydroxy methyl group, which has been shown to be a very powerful structural unit in several chiral auxiliaries.[13]

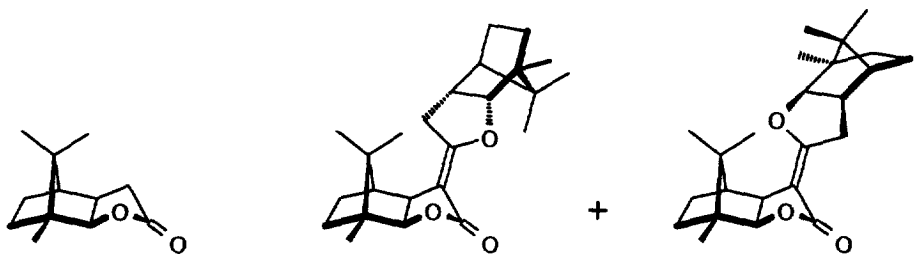
The reaction of **7** with secondary amines in the presence of aluminum chloride[14] led to the corresponding amides **9a–g** which could easily be reduced by lithium aluminum hydride to the δ-aminoalcohols **10a–g**. Whereas diethylamine and diisobutylamine react nearly quantitatively using a molar ratio of

Table 1
Summary of synthesized amides **9** and aminoalcohols **10**

9, 10	R1	R2	Yield (%) 9	Yield (%) 10	9, 10	R1, R2	Yield (%) 9	Yield (%) 10
a	Et	Et	97	97	f		72	87
b	*i*-Bu	*i*-Bu	95	87				
c	Me	Ph	37	85	g		60	88
d	Me	1-Napht	12	82				
e	Bn	Bn	65	98				

7/$AlCl_3$/amine=1/1.3/2.5 the yields in the synthesis of the *N*-aryl-alkyl derivatives were significantly lower. Although the ratio of **7**/$AlCl_3$/amine was changed to 1/2/4, **9c** and **9d** were obtained with yields of only 37 and 12%, respectively. This may be due to the lower basicity and nucleophilic strength of this type of amine.[15] The reduced reactivity of the cyclic amines, morpholine and *S*-prolinol methylether may be attributed to the additional heteroatom present in the amine. This offers a further position for complexation of $AlCl_3$ and thus diminishes the effective quality of catalyst. Reduction of the amides **9a–g** with lithium aluminum hydride gave the amino alcohols **10a–g** in good to excellent yield.

When using aliphatic amines with steric hindrance like diisopropylamine, no amide was formed but instead a Lewis acid catalyzed aldol condensation took place which afforded the diastereomeric adducts **11a** and **11b** after chromatographic separation in a ratio of 9/1 (Scheme 2).



7 **11a** **11b**

Scheme 2. Aldol condensation of **7** gives diastereomeric adducts **11a** and **11b**

An X-ray structure determination of **11a** was carried out. Crystal data: $C_{24}H_{34}O_3$, M_r=370.51, orthorhombic, space group $P2_12_12_1$ (No. 19), a=7.146(3) Å, b=10.258(5) Å, c=28.067(10) Å, V=2057(2) Å^3, Z=4, Dx=1.196 g cm^{-3}, λ=0.71073 Å, μ=0.077 mm^{-1}, T=300 K. A colorless block of 0.7×0.4×0.35 mm was used for data collection with a Siemens Smart CCD area-detector-platform-type diffractometer and Mo Kα radiation from a sealed X-ray tube. Intensity data ($\theta \leq 25°$) were gathered over more than one hemisphere of the reciprocal space using 0.3° ω-scan frames. Data were corrected for Lp, decay, absorption and related effects with an empirical method using the program SADABS;[16] 11 900 reflections collected, 3628 independent, R_{int}=0.024. The structure was solved with direct methods and was refined with the program SHELXL97.[17,18] Hydrogen atoms were located according to a difference Fourier map

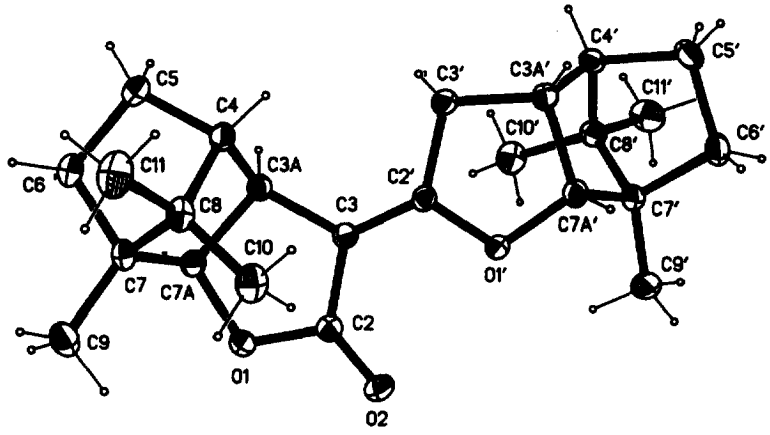


Figure 2. X-Ray structure of **11a**

and were refined riding with the atoms to which they had bonded. The absolute configuration of the structure was adopted from the camphor moiety. The final refinement varied 251 parameters and used all 3628 independent reflections weighted by $w=1/[\sigma^2(F_o^2)+(0.048P)^2+0.22P]$ where $P=(F_o^2+2F_c^2)/3$. Final $R1=\sum||F_o|-|F_c||/\sum|F_o|=0.040$, $wR2=[\sum(w(F_o^2-F_c^2)^2)/\sum(w(F_o^2)^2)]^{1/2}=0.089$ and $S=1.04$ for all data; $R1=0.034$ for the 3253 reflections with $F_o^2>2\sigma(F_o^2)$; deviations in final difference Fourier map between -0.125 and 0.124 e $Å^{-3}$.[19]

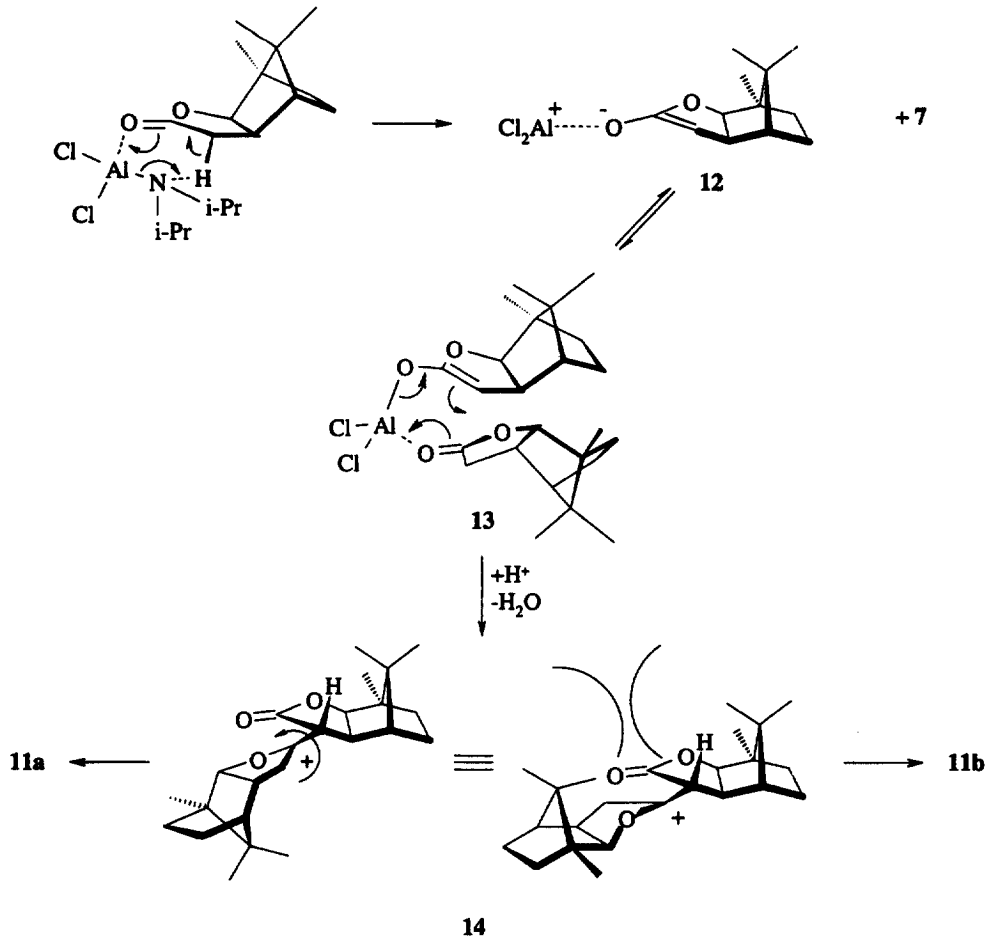
A view of the molecular structure of **11a** is given in Fig. 2. The crystal structure analysis proved the compound to be the *Z*-isomer. Bond lengths and bond angles are consistent with the structural formula. The furanylidene–furanone ring system is essentially flat showing an r.m.s deviation of only 0.042 Å from a common least-squares plane. This part of the molecule is closely related to the cardiotoxic carolic acid, (*E,R*)-5-methyl-3-(2′-tetrahydrofurylidene)-tetrahydrofuran-2,4-dione.[20] In contrast to **11a**, where the camphor moiety causes the tetrahydrofurylidene ring to be flat, the corresponding ring in carolic acid shows a moderate puckering with an envelope conformation for one CH_2 group.

The selectivity observed in the formation of **11a** and **11b**, respectively, may be rationalized by the chelated transition state **13** (Zimmermann–Traxler),[21] as well as the different conformations of **14**, which should be formed as an intermediate assuming an E1-mechanism for the elimination of water (Scheme 3).

3. Experimental section

3.1. General

Melting points are uncorrected. IR: Perkin–Elmer System 2000 FT-IR. NMR: Bruker AC 200 (200 and 50 MHz, for ^1H and ^{13}C, respectively). For ^1H NMR TMS at $\delta_H=0.00$ or $CHCl_3$ at $\delta_H=7.24$ as internal standards; for ^{13}C NMR TMS at $\delta_C=0.00$ or $CDCl_3$ at $\delta_C=77.0$ as internal standards. Optical rotations were measured with a Perkin–Elmer 241 polarimeter in a 10 cm cell. TLC was performed with Merck silica gel 60 F_{254}; with visualization of the spots with molybdato phosphoric acid (5% in ethanol) and heating. Column chromatography and vacuum flash chromatography (VFC) was carried out with Merck silica gel 60 (230–400 mesh). Abbreviations used: PE=petroleum ether.



Scheme 3. Possible reaction pathway explaining the preferred formation of **11a**

3.2. *Synthesis of [1R-(2exo,3exo)]-3-hydroxy-4,7,7-trimethylbicyclo[2.2.1]heptane-2-ethanol* **8a**

To a suspension of 3.00 g (79 mmol) of lithium aluminum hydride in 200 ml of anhydrous diethyl ether, 10.22 g (52.61 mmol) of **7** dissolved in 30 ml of anhydrous ether was added dropwise at room temperature at such a rate that the reaction mixture was kept at reflux. After an additional hour at reflux the reaction mixture was quenched with ice–water and 15% sulfuric acid until the solution became clear. The aqueous layer was extracted with ether. The combined organic layers were washed with brine, dried with sodium sulfate, filtered and the solvent was evaporated. Yield: 10.3 g (99%) of colourless crystals. Mp=105°C (*n*-hexane), R_f (PE/Et_2O=1/1)=0.25, $[\alpha]_D^{20}$=+0.34 (*c* 2.43, CH_2Cl_2); $C_{12}H_{22}O_2$ (198.31): calculated: C 72.68, H 11.18; found: C 72.93, H 11.35; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.75 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 0.92–1.12 (m, 2H, 5-H_{endo}, 6-H_{endo}), 1.33–1.79 (m, 5H, 1-H, 5-H_{exo}, 6-H_{exo}, β-H_A, –OH), 2.05–2.24 (m, 1H, β-H_B), 3.49 (ddd, 1H, 2-H), 3.67–3.80 (m, 4H, α-H, 3-H, –OH); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.5 (q, C-10), 21.1/21.5 (2q, C-7/C-8), 29.5 (t, C-6), 32.8 (t, C-5), 33.4 (t, C-β), 46.2 (s, C-7), 49.0 (s, C-4), 50.1 (d, C-1), 52.0 (d, C-2), 63.2 (t, C-α), 80.6 (d, C-3).

3.3. Synthesis of [1R-(2exo,3exo)]-3-hydroxy-α,α-diphenyl-1,7,7-trimethylbicyclo[2.2.1]heptane-ethanol 8b

To a solution of 24 ml (38.6 mmol) phenyllithium (1.6 M in cyclohexane/ether), 3.0 g (15.4 mmol) of **7** dissolved in 30 ml of anhydrous THF was added dropwise between −5 and 10°C over a period of 10 min. After stirring the reaction mixture for an additional 7 h at room temperature, 20 ml of ice–water was added at 0°C. The THF was evaporated in vacuo and the residue was extracted with ether. The combined organic layers were washed with water, dried with sodium sulfate, filtered and concentrated under reduced pressure. The crude product (5.480 g of a yellow oil) was purified with VFC (120 g silica gel, gradient of PE/Et_2O=6/1 to 1/1). The colourless foam thus obtained was crystallized from *n*-hexane. Yield: 4.034 g (75%) of colourless crystals. Mp=111°C (*n*-hexane), R_f (PE/Et_2O=2/1)=0.26, $[\alpha]_D^{20}$=+75.3 (*c* 1.10, CH_2Cl_2); $C_{24}H_{30}O_2$ (350.51): calculated: C 82.24, H 8.63; found: C 82.11, H 8.66; ^{1}H NMR (200 MHz; $CDCl_3$, D_2O): δ_H=0.73–1.08 (m, 2H, 5-H_{endo}, 6-H_{endo}), 0.79 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 1.33–1.73 (m, 3H, 5-H_{exo}, 6-H_{exo}, 1-H), 1.83 (dd, 1H, J_{AX}=10.8 Hz, 2-H), 2.50 (dd, 1H, J_{BX}=2.1 Hz, β-H_B), 2.93 (dd, 1H, J_{AB}=14.8 Hz, β-H_A), 3.66 (d, 1H, *J*=8.2 Hz, 3-H), 7.12–7.54 (m, 10H, aromatic-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.7 (q, C-10), 21.6/21.9 (2q, C-7/C-8), 29.6 (t, C-6), 33.4 (t, C-5), 42.1 (t, C-β), 45.8 (d, C-2), 46.8 (s, C-7), 49.5 (s, C-4), 53.5 (d, C-1), 78.6 (s, C-α), 81.6 (d, C-3), 125.8/126.4/126.6 (3d, 6C, *ortho*-C, *para*-C), 128.0 (d, 4C, *meta*-C), 146.1/149.4 (2s, 2C, *ipso*-C).

3.4. General procedure (GP-1) for the synthesis of the amides 9a–g

A solution of the secondary amine in 1,2-dichloroethane was added to a suspension of $AlCl_3$ in 1,2-dichloroethane under external cooling and vigorous stirring. The temperature of the reaction mixture was maintained at 15–25°C during the addition. After an additional 30 min the cooling bath was removed and the solid lactone **7** was added in one portion. The reaction mixture was quenched with a mixture of ice and water under external cooling, stirred for 30 min and the aqueous layer extracted 3 times with dichloromethane. The combined organic layers were extracted twice with 2 N HCl, washed with water, dried with Na_2SO_4, filtered and the solvent was evaporated. The crude product was purified by distillation or VFC.

3.4.1. [1R-(2exo,3exo)]-N,N-Diethyl-3-hydroxy-4,7,7-trimethylbicyclo[2.2.1]heptane-acetamide 9a

Following GP-1, **9a** was prepared from 4.710 g (64.3 mmol) of diethylamine (in 15 ml 1,2-dichloroethane), 4.46 g (33.5 mmol) of $AlCl_3$ (in 15 ml 1,2-dichloroethane) and 5.000 g (25.7 mmol) of **7**. The reaction mixture was stirred for 60 h at room temperature. The crude product was slightly yellow and was purified by Kugelrohr distillation. Yield: 6.676 g (97%) of a colourless oil. Bp=80°C/0.005 torr (Kugelrohr), R_f (PE/Et_2O=1/1)=0.21, $[\alpha]_D^{20}$=+43.9 (*c* 0.70, CH_2Cl_2); $C_{16}H_{29}NO_2$ (267.41): calculated: C 71.87, H 10.93, N 5.24; found: C 71.72, H 11.10, N 5.24; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.79 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 1.01–1.30 (m, 11H, 3×CH_3, 5-H_{endo}, 6-H_{endo}), 1.34–1.85 (m, 3H, 1-H, 5-H_{exo}, 6-H_{exo}), 2.01 (2dd, 1H, J_{AX}=3.5 Hz, 2-H), 2.54 (dd, 1H, J_{AB}=15.4 Hz, α-H_A), 2.80 (dd, 1H, J_{BX}=12.4 Hz, α-H_B), 3.22–3.47 (m, 4H, 2×–NCH_2), 3.74 (s, 1H, OH), 3.84 (d, 1H, *J*=7.6 Hz, 3-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.7 (q, C-10), 12.9/14.3 (2q, 2×–CH_2CH_3), 21.6/22.0 (2q, C-8/C-9), 29.7 (t, C-6), 33.6/33.8 (2t, C-5, C-α), 40.4/42.4 (2t, 2×NCH_2), 46.9 (s, C-7), 47.7 (d, C-2), 49.2 (s, C-4), 51.3 (d, C-1), 80.8 (d, C-3), 173.7 (s, –C=O).

3.4.2. [1R-(2exo,3exo)]-3-Hydroxy-4,7,7-trimethyl-N,N-di(2-methylpropyl)bicyclo[2.2.1]-heptane-acetamide ***9b***

Following GP-1, **9b** was prepared from 3.327 g (25.7 mmol; 4.50 ml) of diisobutylamine (in 4 ml 1,2-dichloroethane), 1.789 g (13.4 mmol) of $AlCl_3$ (in 6 ml 1,2-dichloroethane) and 2.000 g (10.3 mmol) of **7**. The reaction mixture was stirred for 18 h at room temperature. The crude product (3.1 g of a red oil) was purified by VFC (60 g silica gel, PE/Et_2O=2/1). Yield: 3.078 g (95%) of a colourless oil. Bp=80°C/0.01 torr (Kugelrohr), R_f (PE/Et_2O=2/1)=0.31, $[\alpha]_D^{20}$=+68.02 (*c* 3.50, CH_2Cl_2); $C_{20}H_{37}NO_2$ (323.52): calculated: C 74.25, H 11.53, N 4.33; found: C 74.15, H 11.27, N 4.47; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.74 (s, 3H, CH_3), 0.78–0.90 (m, 15H, 5×CH_3), 0.96–1.08 (m, 2H, 5-H_{endo}, 6-H_{endo}), 1.11 (s, 3H, CH_3), 1.29–2.04 (m, 6H, 1-H, 2-H, 5-H_{exo}, 6-H_{exo}, 2×–C*H*Me_2), 2.53 (dd, 1H, J_{AB}=15.4 Hz, J_{BX}=3.7 Hz, α-H_B), 2.76 (dd, 1H, J_{AX}=12.0 Hz, α-H_A), 2.97–3.23 (m, 4H, 2×–N–CH_2iPr), 3.65 (bs, 1H, OH), 3.77 (d, 1H, *J*=7.7 Hz, 3-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.8 (q, C-10), 20.0/20.1/21.6/22.0 (4q, 6C, 6×CH_3), 26.5/28.0 (2d, 2×–*C*HMe_2), 29.7 (t, C-6), 33.6/34.2 (2t, C-5, C-α), 46.9 (s, C-7), 47.9 (d, C-2), 49.2 (s, C-4), 51.4 (d, C-1), 53.4/55.9 (2t, 2×–CH_2-i-Pr), 80.9 (d, C-3), 174.9 (s, C=O).

3.4.3. [1R-(2exo,3exo)]-3-Hydroxy-N,4,7,7-tetramethyl-N-phenyltrimethylbicyclo[2.2.1]-heptane-acetamide ***9c***

Following GP-1, **9c** was prepared from 44.1 g (411.6 mmol) of *N*-methylaniline (in 40 ml 1,2-dichloroethane), 27.5 g (205.8 mmol) of $AlCl_3$ (in 70 ml 1,2-dichloroethane) and 20.000 g (102.9 mmol) of **7**. The reaction mixture was stirred for 60 h at room temperature. The crude product was recrystallized from *n*-hexane and the mother liquor was purified by VFC (200 g silica gel, gradient of PE/Et_2O=3/1 to MeOH). Yield: 11.46 g (37%) of pale violet crystals. Mp=110°C (*n*-hexane), R_f (PE/Et_2O=4/1)=0.21, $[\alpha]_D^{20}$=+75.00 (*c* 2.06, CH_2Cl_2); $C_{19}H_{27}NO_2$ (301.43): calculated: C 75.71, H 9.03, N 4.65; found: C 75.69, H 9.10, N 4.57; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.60–1.80 (m, 14H, 1-H, 5-H, 6-H, 3×CH_3), 1.90–2.04 (m, 1H, 2-H), 2.12–2.35 (m, 1H, α-H_A), 2.50–2.73 (m, 1H, α-H_B), 3.26 (s, 3H, –NCH_3), 3.70 (bs, 1H, OH), 3.83 (d, 1H, *J*=6.3 Hz, 3-H), 7.01–7.50 (m, 5H, aromatic-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.8 (q, C-10), 21.3/22.0 (2q, C-8, C-9), 29.7 (t, C-6), 33.6 (t, C-5), 34.8 (t, C-α), 37.3 (q, –NCH_3), 46.8 (s, C-7), 48.0 (d, C-2), 49.2 (s, C-4), 51.0 (d, C-1), 80.8 (d, C-3), 127.0 (d, 2C, *ortho*-C), 127.7 (d, *para*-C), 129.7 (d, 2C, *meta*-C), 144.0 (s, *ipso*-C), 174.6 (s, –C=O).

3.4.4. [1R-(2exo,3exo)]-3-Hydroxy-N,4,7,7-tetramethyl-N-(naphthalin-1-yl)bicyclo[2.2.1]-heptane-acetamide ***9d***

Following GP-1, **9d** was prepared from 22.66 g (144.1 mmol) of *N*-methyl-1-naphthylamine (in 20 ml 1,2-dichloroethane), 9.608 g (72.1 mmol) of $AlCl_3$ (in 40 ml 1,2-dichloroethane) and 7.000 g (36.0 mmol) of **7**. The reaction mixture was stirred for 78 h at 50°C. After quenching, the mixture was filtered through Celite, concentrated in vacuo and the residue dissolved in Et_2O. After workup according to GP-1, the crude product (8.985 g, dark oil) was purified by VFC (400 g silica gel, gradient of PE/Et_2O=3/1 to Et_2O). Yield: 1.500 g (12%) of colourless crystals. Mp=146°C (2-propanol), R_f (PE/Et_2O=3/1)=0.05, $[\alpha]_D^{20}$=+60.2 (*c* 3.50, CH_2Cl_2); $C_{23}H_{29}NO_2$ (351.49): calculated: C 78.60, H 8.32, N 3.98; found: C 78.43, H 8.34, N 3.89; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.61 (s, 3H, CH_3), 0.83 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.80–1.70 (m, 5H, 1-H, 5-H, 6-H), 1.90–2.24 (m, 2H, α-H_B, 2-H), 2.41–2.70 (m, 1H, α-H_A), 3.35 (s, 3H, N–CH_3), 3.66 (s, 1H, OH), 3.84 (d, 1H, *J*=7.4 Hz, 3-H), 7.25–8.03 (m, 7H, aromatic-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.8 (q, C-10), 21.2/21.8 (2q, C-8, C-9), 29.6 (t, C-6), 33.6 (t, C-α), 34.7 (t, C-5), 37.1 (d, C-2), 46.7 (s, C-7), 48.1 (d, C-1), 49.2 (s, C-4), 50.8 (q, N–CH_3), 80.9 (d, C-3), 122.2/124.9/125.8/126.8/127.3/127.5/128.6/129.9/134.7/140.2 (10C, aromatic-C), 175.4 (s, C=O).

3.4.5. [1R-(2exo,3exo)]-3-Hydroxy-4,7,7-trimethyl-N,N-di(phenylmethyl)bicyclo[2.2.1]-heptane-acetamide ***9e***

Following GP-1, **9e** was prepared from 17.771 g (90.1 mmol) of dibenzylamine (in 18 ml 1,2-dichloroethane), 6.246 g (46.8 mmol) of $AlCl_3$ (in 11 ml 1,2-dichloroethane) and 7.000 g (36.0 mmol) of **7**. The reaction mixture was stirred for 48 h at room temperature. The crude product (17.007 g) was treated with CH_2Cl_2 and PE to remove crystalline dibenzylamine hydrochloride. The mother liquor was purified by VFC (200 g silica gel, PE/Et_2O=3/1). Yield: 9.113 g (65%) of colourless crystals. Mp=126°C ($CHCl_3$/*n*-hexane), R_f (PE/Et_2O=3/1)=0.20, $[\alpha]_D^{20}$=+53.5 (*c* 0.80, CH_2Cl_2); $C_{26}H_{33}NO_2$ (391.56): calculated: C 79.76, H 8.50, N 3.58; found: C 79.55, H 8.37, N 3.55; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.79 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 0.88–1.25 (m, 2H, 5-H_{endo}, 6-H_{endo}), 1.39–1.83 (m, 3H, 1-H, 5-H_{exo}, 6-H_{exo}), 2.18 (2dd, 1H, J_{AX}=11.8 Hz, 2-H), 2.64 (dd, 1H, J_{BX}=3.9 Hz, α-H_B), 2.99 (dd, 1H, J_{AB}=15.8 Hz, α-H_A), 3.37 (s, 1H, OH), 3.93 (d, 1H, *J*=7.8 Hz, 3-H), 4.42–4.77 (m, 4H, 2×–CH_2Ph), 7.10–7.48 (m, 10H, aromatic-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.8 (q, C-10), 21.5/22.0 (2q, C-8, C-9), 29.6 (t, C-6), 33.6 (t, C-5), 34.1 (t, C-α), 46.9 (s, C-7), 47.3 (s, C-2), 48.3 (d, *cis*-CH_2–Ph), 49.3 (s, C-4), 50.2 (t, *trans*-CH_2–Ph), 51.0 (d, C-1), 81.0 (d, C-3), 126.4/127.3/127.5/128.1/128.5/128.8 (10C, *ortho*-C, *meta*-C, *para*-C), 136.4/137.2 (2s, *ipso*-C), 175.1 (s, C=O).

3.4.6. [1R-(2exo,3exo)]-1-[(3-Hydroxy-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl)acetyl]-2-(methoxymethyl)pyrrolidine ***9f***

Following GP-1, **9f** was prepared from 7.410 g (64.3 mmol) of prolinol-methyl ether (in 10 ml 1,2-dichloroethane), 4.460 g (33.4 mmol) of $AlCl_3$ (in 15 ml 1,2-dichloroethane) and 5.000 g (25.7 mmol) of **7**. The reaction mixture was stirred for 36 h at 60°C. The crude product (7.847 g, yellow oil) was purified by VFC (160 g silica gel, gradient of PE/Et_2O=1/1 to Et_2O). Yield: 5.753 g (18.6 mmol, 72%) of a colourless oil. Bp=95°C/0.01 torr (Kugelrohr), R_f (PE/Et_2O=1/2)=0.24, $[\alpha]_D^{20}$=+35.03 (*c* 2.58, CH_2Cl_2); $C_{18}H_{31}NO_3$ (309.45): calculated: C 69.87, H 10.10, N 4.53; found: C 69.57, H 9.91, N 4.61; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.40–2.20 (m, 19H, 1-H, 2-H, 5-H, 6-H, 3′-H, 4′-H, 3×CH_3), 2.28–2.94 (m, 2H, 5′-H), 3.05–4.50 (m, 10H, 3-H, α-H, 2′-H, –CH_2OMe, –OCH_3, OH); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.7 (q, C-10), 21.5/21.9 (2q, C-8, C-9), 23.8/27.4/28.6/29.5/33.6/35.1/35.8 (7t, 5C, C-5, C-6, C-α, C-3′, C-4′), 45.6/46.8 (2t, 1C, C-5′), 47.2 (s, C-7), 47.4/48.2 (2d, 1C, C-2), 49.1 (s, C-4), 51.0/51.5 (2d, 1C, C-1), 56.2/57.2 (2d, 1C, C-2′), 58.8/59.0 (2q, 1C, –OCH_3), 71.9/74.3 (2t, 1C, C-α), 80.5/80.8 (2d, 1C, C-3), 173.2/173.9 (2s, 1C, C=O).

3.4.7. [1R-(2exo,3exo)]-4-[(3-Hydroxy-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl)acetyl]-morpholine ***9g***

Following GP-1, **9g** was prepared from 11.211 g (129.0 mmol) of morpholine (in 16 ml 1,2-dichloroethane), 8.923 g (66.9 mmol) of $AlCl_3$ (in 26 ml 1,2-dichloroethane) and 10.000 g (51.5 mmol) of **7**. The reaction mixture was stirred for 36 h at room temperature. The crude product (13.6 g, red oil) was purified by VFC (350 g silica gel, gradient of PE/Et_2O=3/1 to 1/1). Yield: 8.650 g (30.7 mmol, 60%) of colourless crystals. Mp=77°C (DIPE), R_f (PE/Et_2O=3/2)=0.11, $[\alpha]_D^{20}$=+66.4 (*c* 1.72, CH_2Cl_2); $C_{16}H_{27}NO_3$ (281.40): calculated: C 68.29, H 9.67, N 4.98; found: C 68.50, H 9.55, N 4.94; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.78 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.97–1.20 (m, 5H, CH_3, 5-H_{endo}, 6-H_{endo}), 1.33–1.81 (m, 3H, 1-H, 5-H_{exo}, 6-H_{exo}), 2.09 (2dd, 1H, J_{AX}=3.9 Hz, 2-H), 2.49 (dd, 1H, J_{AB}=15.8 Hz, α-H_A), 2.80 (dd, 1H, J_{BX}=11.6 Hz, α-H_B), 3.05 (bs, 1H, OH), 3.38–3.72 (m, 8H, 2′-H, 3′-H, 5′-H, 6′-H), 3.82 (d, 1H, *J*=7.8 Hz, 3-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.7 (q, C-10), 21.5/21.9 (2q, C-8/C-9), 29.6 (t, C-6), 33.5/33.6 (2t, C-5, C-α), 41.8 (t, C-2′), 46.0 (t, C-6′), 46.8 (s, C-7), 46.8 (d, C-2), 49.2 (s, C-4), 51.0 (d, C-1), 66.4/66.7 (2t, C-3′, C-5′), 80.8 (d, C-3), 173.0 (s, –C=O).

3.5. General procedure (GP-2) for the synthesis of the aminoalcohols **10a–g**

A solution of **9a–g** in Et_2O was added dropwise to a suspension of lithium aluminum hydride in anhydrous ether at such a rate that reflux was maintained. After heating for one further hour the mixture was cooled and quenched with ice and water. Potassium sodium tartrate was added and the mixture was stirred for 30 min. The aqueous layer was extracted three times with ether and the combined organic layers were extracted with 2 N HCl. The combined HCl layers were basified and extracted three times with ether. The combined organic layers were dried with sodium sulfate, filtered and the solvent evaporated. Purification of the crude amines **10a–g** was performed by distillation.

3.6. [1R-(2exo,3exo)]-3-[2-(Diethylamino)ethyl]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol **10a**

Following GP-2, **10a** was prepared from 6.670 g (25.0 mmol) of **9a** and 1.800 g (50.0 mmol) of $LiAlH_4$ in 50 ml of ether. After workup with 10.000 g (35.4 mmol) of potassium sodium tartrate, the crude product was purified by distillation. Yield: 6.165 g (97%) of colourless crystals. Bp=80°C/0.005 torr (Kugelrohr), mp=37°C, R_f (PE/Et_2O=1/2)=0.12, $[\alpha]_D^{20}=-27.7$ (*c* 0.81, CH_2Cl_2); $C_{16}H_{31}NO$ (253.43): calculated: C 75.83, H 12.33, N 5.53; found: C 76.12, H 12.44, N 5.30; ^1H NMR (200 MHz; $CDCl_3$): δ_H=0.77 (s, 3H, CH_3), 0.89–1.24 (m, 14H, 4×CH_3, 5-H_{endo}, 6-H_{endo}), 1.31–1.81 (m, 5H, 3-H, 4-H, 5-H_{exo}, 6-H_{exo}, β-H_A), 1.91–2.17 (m, 1H, β-H_B), 2.22–2.51 (m, 4H, α-H, –NCH_2), 2.53–2.76 (m, 2H, –NCH_2), 3.66 (d, 1H, *J*=7.4 Hz, 2-H), 6.81 (bs, 1H, –OH); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.3 (q, 2C, 2×–CH_2CH_3), 12.0 (q, C-10), 21.7/22.1 (2q, C-8/C-9), 30.0 (t, C-5), 30.1 (t, C-β), 33.8 (t, C-6), 46.4 (s, C-7), 47.6 (t, 2C, 2×NCH_2), 49.2 (s, C-1), 52.7 (d, C-4), 54.7 (d, C-3), 55.0 (t, C-α), 79.8 (d, C-2).

3.6.1. [1R-(2exo,3exo)]-3-[2-[N,N-Di(2-methylpropylamino)]ethyl]-1,7,7-trimethylbicyclo[2.2.1]-heptan-2-ol **10b**

Following GP-2, **10b** was prepared from 10.000 g (31.9 mmol) of **9b** and 2.421 g (63.8 mmol) of $LiAlH_4$ in 150 ml of ether. After workup with 7.000 g (37.4 mmol) of potassium sodium tartrate, the crude product was purified by distillation. Yield: 8.603 g (87%) of a colourless oil. Bp=80°C/0.005 torr (Kugelrohr), R_f (PE/Et_2O=3/1)=0.46, $[\alpha]_D^{20}=-49.29$ (*c* 1.98, CH_2Cl_2); $C_{20}H_{39}NO$ (309.54): calculated: C 77.61, H 12.70, N 4.53; found: C 77.42, H 12.44, N 4.82; ^1H NMR (200 MHz; $CDCl_3$): δ_H=0.68–1.27 (m, 23H, 7×CH_3, 5-H_{endo}, 6-H_{endo}), 1.30–2.50 (m, 14H, 3-H, 4-H, 5-H_{exo}, 6-H_{exo}, α-H, β-H, 2×–$CHMe_2$, 2×–N–CH_2iPr), 3.64 (d, 1H, *J*=7.1 Hz, 2-H), 4.47 (bs, 1H, –OH); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=12.0 (q, C-10), 21.4/21.6/21.7/22.2 (4q, 6C, 6×CH_3), 26.2 (d, 2C, 2×–$CHMe_2$), 28.7 (t, C-5), 30.0 (t, C-β), 33.8 (t, C-6), 46.5 (s, C-7), 49.4 (s, C-1), 52.0 (d, C-4), 52.8 (d, C-3), 57.7 (t, C-α), 64.5 (t, 2C, 2×–N–CH_2iPr), 80.4 (d, C-2).

3.6.2. [1R-(2exo,3exo)]-3-[2-(N-Methyl-N-phenylamino)ethyl]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol **10c**

Following GP-2, **10c** was prepared from 8.000 g (26.5 mmol) of **9c** and 3.000 g (79.6 mmol) of $LiAlH_4$ in 100 ml of ether. After workup with 16.000 g (85.5 mmol) of potassium sodium tartrate, the crude product was purified by distillation. Yield: 6.506 g (85%) of colourless crystals. Bp=95–100°C/0.005 torr (Kugelrohr), mp=44°C, R_f (PE/Et2O=3/1)=0.54. **10c**·HCl: mp=129–134°C (Et_2O/CH_2Cl_2), $[\alpha]_D^{20}=+29.2$ (*c* 1.90, CH_2Cl_2); $C_{19}H_{30}ClNO$ (323.91): calculated: C 70.46, H 9.34, N 4.32; found: C 70.46, H 9.38, N 4.29; ^1H NMR of **10c** (200 MHz; $CDCl_3$): δ_H=0.82 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 1.00–1.20 (m, 5H, CH_3, 5-H_{endo}, 6-H_{endo}), 1.39–1.87 (m, 5H, 3-H, 4-H, 5-H_{exo}, 6-H_{exo}, β-H_A), 2.02–2.35 (m, 2H, β-H_B, OH), 2.92 (s, 3H, –NCH_3), 3.22–3.41 (m, 2H, α-H), 3.72 (d,

1H, *J*=7.6 Hz, 2-H), 6.68–6.87 (m, 3H, *ortho*-H, *para*-H), 7.26 (dd, 2H, *meta*-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.7 (q, C-10), 21.5/22.1 (2q, C-8, C-9), 27.8 (t, C-5), 29.9 (t, C-β), 33.6 (t, C-6), 38.5 (q, $-NCH_3$), 46.7 (s, C-7), 49.1 (d, C-4), 49.6 (s, C-1), 51.1 (d, C-3), 54.7 (t, C-α), 81.4 (d, C-2), 113.0 (d, 2C, *ortho*-C), 116.7 (d, *para*-C), 129.1 (d, 2C, *meta*-C), 149.8 (s, *ipso*-C).

3.6.3. [1R-(2exo,3exo)]-3-[2-(N-Methyl-N-naphthalin-1-ylamino)ethyl]-1,7,7-trimethylbicyclo[2.2.1]-heptan-2-ol ***10d***

Following GP-2, **10d** was prepared from 1.500 g (4.2 mmol) of **9d**, which was added in solid form to a suspension of 319 mg (8.4 mmol) of $LiAlH_4$ in 20 ml of ether. After workup with 1.000 g (3.5 mmol) of potassium sodium tartrate and extraction with 6 N HCl the crude product was purified by distillation. Yield: 1.143 g (82%) of a colourless oil. Bp=125°C/0.005 torr (Kugelrohr), R_f (PE/Et_2O=2/1)=0.65; $[\alpha]_D^{20}$=+20.0 (*c* 2.38, CH_2Cl_2); $C_{23}H_{31}NO$ (337.51): calculated: C 81.85, H 9.26, N 4.15; found: C 81.71, H 8.97, N 4.29; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.73–1.12 (m, 2H, 5-H_{endo}, 6-H_{endo}), 0.83 (s, 3H, CH_3), 0.97 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.30–2.10 (m, 5H, 3-H, 4-H, 5-H_{exo}, 6-H_{exo}, β-H_A), 2.11–2.39 (m, 1H, β-H_B), 2.60 (bs, 1H, –OH), 2.90 (s, 3H, N–CH_3), 3.09–3.30 (m, 2H, α-H), 3.72 (d, 1H, *J*=7.5 Hz, 2-H), 7.10–8.40 (m, 7H, aromatic-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.8 (q, C-10), 21.5/22.0 (2q, C-8, C-9), 28.2 (t, C-5), 29.8 (t, C-β), 33.6 (t, C-6), 42.9 (d, C-4), 46.7 (s, C-7), 49.5 (s, C-1), 49.6 (q, $-NCH_3$), 50.9 (d, C-3), 58.4 (t, C-α), 81.3 (d, C-2), 115.6/123.3/123.8/125.1/125.2/125.6/128.3/129.3/134.8/150.5 (10C, aromatic-C).

3.6.4. [1R-(2exo,3exo)]-3-[2-[Di(phenylmethyl)amino]ethyl]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol ***10e***

Following GP-2, **10e** was prepared from 6.000 g (15.3 mmol) of **9e**, which was added in solid form and 1.163 g (30.7 mmol) of $LiAlH_4$ in 70 ml of ether. After workup with 4.200 g (14.9 mmol) of potassium sodium tartrate, the crude product was purified by distillation. Yield: 5.666 g (98%) of a colourless oil. Bp=100°C/0.005 torr (Kugelrohr), R_f (PE/Et_2O=1/1)=0.58; $[\alpha]_D^{20}$=−15.7 (*c* 1.13, CH_2Cl_2); $C_{26}H_{35}NO$ (377.57): calculated: C 82.71, H 9.34, N 3.71; found: C 82.55, H 9.39, N 3.67; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.81 (s, 3H, CH_3), 0.84–1.08 (m, 5H, CH_3, 5-H_{endo}, 6-H_{endo}), 1.23 (s, 3H, CH_3), 1.37–1.71 (m, 5H, 3-H, 4-H, 5-H_{exo}, 6-H_{exo}, β-H_A), 2.03–2.26 (m, 1H, β-H_B), 2.40–2.53 (m, 2H, α-H), 3.34 (d, 2H, *J*=13.2 Hz, 2×C*H*H–Ph), 3.48 (d, 1H, *J*=7.2 Hz, 2-H), 3.90 (d, 2H, *J*=13.2 Hz, 2×C*H*H–Ph), 7.20–7.48 (m, 10H, aromatic-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=12.0 (q, C-10), 21.6/22.1 (2q, C-8/C-9), 28.4 (t, C-5), 29.8 (t, C-β), 33.7 (t, C-6), 46.5 (s, C-7), 49.3 (s, C-1), 52.0 (d, C-3), 52.7 (d, C-4), 54.4 (t, C-α), 59.0 (t, 2C, 2×CH_2–Ph), 80.3 (d, C-2), 127.1 (d, 2C, *para*-C), 128.2 (d, 4C, *meta*-C), 129.5 (d, 4C, *ortho*-C), 137.8 (s, 2C, *ipso*-C).

3.6.5. [1R-(2exo,3exo)]-3-[2-[2-(Methoxymethyl)pyrrolidin-1-yl]ethyl]-1,7,7-trimethylbicyclo[2.2.1]-heptan-2-ol ***10f***

Following GP-2, **10f** was prepared from 5.000 g (16.2 mmol) of **9f** and 1.230 g (32.4 mmol) of $LiAlH_4$ in 50 ml of ether. After workup with 3.600 g (12.8 mmol) of potassium sodium tartrate, the crude product was purified by distillation. Yield: 4.380 g (87%) of colourless crystals. Bp=60–65°C/0.02 torr (Kugelrohr), mp=45–47°C, R_f (PE/Et_2O=1/1)=0.25; $[\alpha]_D^{20}$=−31.93 (*c* 0.66, CH_2Cl_2); $C_{18}H_{33}NO_2$ (295.47): calculated: C 73.17, H 11.26, N 4.74; found: C 73.11, H 11.05, N 4.99; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.75 (s, 3H, CH_3), 0.80–1.18 (m, 8H, 2×CH_3, 5-H_{endo}, 6-H_{endo}), 1.32–2.15 (m, 11H, 3-H, 4-H, 5-H_{exo}, 6-H_{exo}, β-H_A, α-H, 3′-H, 4′-H), 2.37–2.88 (m, 3H, β-H_B, 5′-H), 3.17–3.48 (m, 6H, 2′-H, $-OCH_3$ at 3.33, $-CH_2$OMe), 3.64 (d, 1H, *J*=7.3 Hz, 2-H), 6.38 (bs, 1H, –OH); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=12.2 (q, C-10), 21.7/22.1 (2q, C-8, C-9), 23.0 (t, C-4′), 28.6 (t, C-3′), 30.0/30.6 (2t, C-5,

C-β), 34.0 (t, C-6), 46.5 (s, C-7), 49.3 (s, C-1), 52.7 (d, C-4), 55.0 (d, C-3), 55.2 (t, C-α), 57.9 (t, C-5′), 58.9 (q, $-OCH_3$), 63.6 (d, C-2′), 76.6 (t, $-CH_2OMe$), 80.1 (d, C-2).

3.6.6. [1R-(2exo,3exo)]-1,7,7-Trimethyl-3-[2-(morpholin-4-yl)ethyl]bicyclo[2.2.1]heptan-2-ol ***10g***

10g was prepared according to Ando[22] from 2.000 g (7.1 mmol) of **9g** and 559 mg (14.7 mmol) of $LiAlH_4$ in 50 ml of anhydrous THF. After workup, the crude product was purified by distillation. Yield: 1.666 g (88%) of colourless crystals. Bp=85°C/0.01 torr (Kugelrohr), mp=85°C (*n*-hexane), R_f (PE/Et_2O=1/1)=0.24; $[\alpha]_D^{20}=-10.7$ (*c* 1.97, CH_2Cl_2); $C_{16}H_{29}NO_2$ (267.41): calculated: C 71.87, H 10.93, N 5.24; found: C 71.72, H 10.68, N 5.21; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.77 (s, 3H, CH_3), 0.86–1.28 (m, 8H, 2×CH_3, 5-H_{endo}, 6-H_{endo}), 1.30–1.80 (m, 5H, 3-H, 4-H, 5-H_{exo}, 6-H_{exo}, β-H_A), 1.90–2.78 (m, 7H, β-H_B, α-H, 2′-H, 6′-H), 3.56–3.87 (m, 5H, 2-H, 3′-H, 5′-H), 5.65 (bs, 1H, –OH); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=12.1 (q, C-10), 21.7/22.1 (2q, C-8, C-9), 28.2 (t, C-5), 30.0/33.9 (2t, C-6, C-β), 46.6 (s, C-7), 49.4 (s, C-1), 52.6 (d, C-3), 54.2/54.4 (2t, C-2′, C-6′), 61.1 (t, C-α), 66.7 (t, C-3′, C-5′), 80.2 (d, C-2).

3.7. [3aS-(3(3aR,4S*,7S*,7aR*),3aα,4β,7β,7aα-(Z))]-Hexahydro-3-(hexahydro-7,8,8-trimethyl-4,7-methanobenzofuran-2(3H)-yliden)-7,8,8-trimethyl-4,7-methanobenzofurane-2(3H)-one* ***11a*** *and [3aS-[3(3aR*,4S*,7S*,7aR*),3aα,4β,7β,7aα-(E))]-hexahydro-3-(hexahydro-7,8,8-trimethyl-4,7-methanobenzofurane-2(3H)-yliden)-7,8,8-trimethyl-4,7-methanobenzofuran-2(3H)-one* ***11b***

Following GP-1, **11a,b** was prepared from 13.000 g (128.7 mmol) of diisopropylamine (in 16 ml 1,2-dichloroethane), 8.920 g (66.9 mmol) of $AlCl_3$ (in 26 ml 1,2-dichloroethane) and 10.000 g (51.5 mmol) of **7**. The reaction mixture was stirred for 1 h at 65°C and for an additional 18 h at room temperature. After workup, the crude product was treated with ethanol to obtain the *Z*-product **11a**. The mother liquor was purified by column chromatography (100 g silica gel, PE/Et_2O=2/1). Eventually, 3.328 g (36%) of **11a** and 423 mg (4%) of **11b** were obtained.

11a: Colourless crystals. Mp=270–271°C ($CHCl_3$/EtOH), R_f (PE/Et_2O=2/1)=0.14; $[\alpha]_D^{20}=-38.0$ (*c* 0.45, CH_2Cl_2); $C_{24}H_{34}O_3$ (370.54): calculated: C 77.80, H 9.25; found: C 77.52, H 9.45; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.68–1.20 (m, 22H, 6×CH_3, 5-H_{endo}, 5′-H_{endo}, 6-H_{endo}, 6′-H_{endo}), 1.33–1.93 (m, 6H, 5-H_{exo}, 5′-H_{exo}, 6-H_{exo}, 6′-H_{exo}, 4-H, 4′-H), 2.28–2.63 (m, 2H, 3a′-H, 3′-H_A), 2.72–3.11 (m, 2H, 3a-H, 3′-H_B), 4.20 (d, 1H, *J*=7.9 Hz, 7a′-H), 4.55 (d, 1H, *J*=7.6 Hz, 7a-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.3 (q, 2C, C-11, C-11′), 19.8/20.4/22.8/23.0 (4q, C-9, C-9′, C-10, C-10′), 28.0/28.5 (2t, C-5, C-5′), 31.8/32.4 (2t, C-6, C-6′), 37.7 (t, C-3′), 43.8 (d, C-3a′), 46.4/46.5/48.9 (3s, 4C, C-7, C-7′, C-8, C-8′), 48.2/49.5 (2d, C-4, C-4′), 48.9 (d, C-3a), 88.0 (d, C-7a), 99.0 (d, C-7a′), 99.0 (s, C-3), 168.4/170.3 (2s, C-2, C-2′).

11b: Colourless crystals. Mp=190°C, R_f (PE/Et_2O=2/1)=0.27; $[\alpha]_D^{20}=-42.3$ (*c* 0.22, CH_2Cl_2); $C_{24}H_{34}O_3$ (370.54): calculated: C 77.80, H 9.25; found: C 77.66, H 9.18; ^{1}H NMR (200 MHz; $CDCl_3$): δ_H=0.69–0.88 (m, 12H, 4×CH_3), 0.90–1.22 (m, 10H, 2×CH_3, 5-H_{endo}, 5′-H_{endo}, 6-H_{endo}, 6′-H_{endo}), 1.35–1.85 (m, 5H, 5-H_{exo}, 5′-H_{exo}, 6-H_{exo}, 6′-H_{exo}, 4′-H), 2.01 (d, 1H, *J*=4.0 Hz, 4-H), 2.40 (2dd, 1H, 3a′-H), 2.90–3.11 (m, 2H, 3a-H, 3′-H_A), 3.17–3.40 (m, 1H, 3′-H_B), 4.18 (d, 1H, *J*=7.8 Hz, 7a-H), 4.33 (d, 1H, *J*=7.8 Hz, 7a′-H); ^{13}C NMR (50 MHz; $CDCl_3$): δ_C=11.3/11.6 (q, 2C, C-11, C-11′), 20.1/20.3/22.8/23.0 (4q, C-9, C-9′, C-10, C-10′), 28.1/28.5 (2t, C-5, C-5′), 32.0/32.5 (2t, C-6, C-6′), 36.8 (t, C-3′), 44.9 (d, C-3a′), 46.5/48.4/48.9 (3s, C-7, C-7′, C-8, C-8′), 47.4 (d, C-4), 47.8 (d, C-3a), 49.6 (d, C-4′), 88.5 (d, C-7a), 97.2 (d, C-7a′), 99.9 (s, C-3), 171.0/174.0 (2s, C-2, C-2′).

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