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Highly diastereoselective synthesis of new optically active aminoalcohols in one step from (+)-camphor and (−)-fenchone

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Abstract: New optically active aminoalcohols have been prepared from $CeCl_3$-activated (+)-camphor and (−)-fenchone and N-functionalized organolithium compounds. The aminoalcohols obtained catalyze the addition of diethylzinc to benzaldehyde in high yields and enantioselectivities up to 64%. © 1997 Elsevier Science Ltd

The synthesis of optically active aminoalcohols and their application as catalysts for enantioselective addition reactions of dialkylzinc compounds to aldehydes has been a topic of increased interest in recent years[1]. *Noyori* and co-workers have demonstrated one of the most effective ligands as catalysts, (−)-3-*exo*-(dimethylamino)isoborneol (DAIB), and have suggested an explanation for its catalytic activity and efficiency[2]. The synthesis and application of some other camphor derived aminoalcohols have also been described[3,4] showing the potential importance of the camphor skeleton as a source of chiral information.

The addition of organometallic reagents to (+)-(1*R*)-camphor **1** and (−)-1*R*-fenchone **2** has been the key step in our investigations concerning the synthesis of optically active alcohols[5a,b], diols[5c,d] and epoxyalcohols[5e]. In most of the cases the use of highly active anhydrous $CeCl_3$, prepared by an improved procedure, was necessary for the activation of these ketones, providing an excellent addition of a variety of organometallics[5a,6]. With the addition of N,N-dimethylaminopropyl lithium **3** to **1** and **2** we demonstrated[5a] a useful one-step synthetic procedure for the preparation of aminoalcohols **8** and **13** (Scheme 1). In this paper we report on the preparation of new chiral aminoalcohols *via* the addition of N-functionalized organolithium compounds to **1** and **2** respectively, as well as their application as catalysts for the addition of diethylzinc to benzaldehyde.

The ketones **1** and **2** were first of all stirred for 0.5 h in THF with anhydrous $CeCl_3$, prepared by our improved drying procedure[5a,6]. The addition of N,N-dimethylaminopropyl-lithium[7] **3**, 2-N,N-dimethylaminophenyl-lithium TMEDA-complex[8] **4**, N-methylpyrrol-2-yl-lithium[8] **6** and N-methylpyrrol-2,5-diyl-dilithium TMEDA-complex[9] **7** occurred at room temperature, resulting in fast reactions with formation of homogeneous reaction mixtures. 2-Pyridyl-lithium[8] **5**, possessing low thermal stability, was prepared and added at −78°C. The compounds **8**, **10**, **11**, **13**, **15** and **16** were isolated in high yields (up to 97%). The aminoalcohol **10** has been previously synthesized[4], in a very low yield however, as the reaction was carried out without the assistance of $CeCl_3$. The addition of reagent **4** was incomplete, most probably as a result of significant steric hindrance of the *o*-positioned dimethylamino group, resulting in low yields of **9** (8%) and **14** (4%). Surprisingly, the formation of *m*- and *p*-dimethylamino substituted addition products[10] in comparable yields, due to the lower steric hindrance, was also observed (see Experimental section), although the content of the corresponding *m*- and *p*-lithiated species in reagent **4** was not significant[11].

The addition products **12** and **17** were obtained in low yields (5% and 10%) and always in a mixture with the monosubstituted derivatives **11** and **16** respectively, which were surprisingly the main products. Therefore, reagent **7** was analysed by reaction with Me_3SiCl followed by NMR investigations, which showed, according to earlier published data[9], that ca. 20% of monolithiated N-methylpyrrole (reagent

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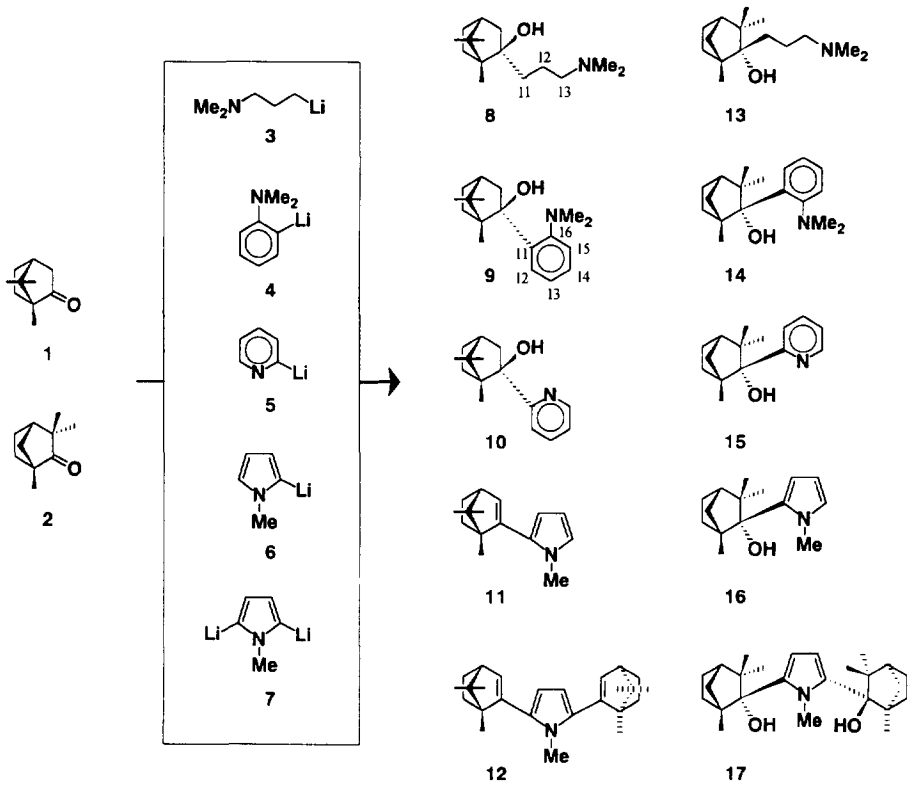

Scheme 1.

6) was present. These observations indicate that the reaction of ketones **1** and **2** with the second lithiated centre of reagent **7** does not proceed completely. Consequently, reagent **7** also serves as a precursor for the monosubstituted products **11** and **16**. In the case of camphor only the olefinic compounds **11** and **12** were obtained, obviously favoured by the formation of a conjugated diene system after water elimination.

The addition reactions were in the case of camphor 100% diastereoselective, in accordance with our previous observations[5a–d]. The unfavourable *endo*-attack to fenchone occurred only during the formation of compounds **16** (*endo*-OH-**16a**/*exo*-OH-**16b**=93:7 by NMR) and **17** (the diastereoisomer was detected, however the content could not be determined). The *exo*-substitution of the major isomer of **16** could be deduced from the strong deshielding of the C-8 methyl carbon (Table 1), similar to previous observations[5b,d]. The observed diastereoselectivities allowed the absolute configuration of the products to be defined (see Experimental section).

The aminoalcohols **8–10** and **13–17** were tested as catalysts (3 mol%) for the addition of diethylzinc to benzaldehyde[12]. In all cases, the yields of the isolated 1-phenyl-1-propanol were high, with the exception of the reaction catalyzed by ligand **16** (Table 2). The enantioselectivities obtained were very low (Entries 9, 10) to moderate (Entries 1–7). Remarkably, in the case of ligand **15** no asymmetric induction was observed irrespectively of the variation of the reaction conditions — temperature or solvent (toluene/hexane or diethyl ether). In this case the zinc alkoxide complex, formed after mixing of ligand **15** with diethylzinc, was highly insoluble. This complex was isolated in the form of colourless crystals, however the attempts for NMR investigations failed because of the insolubility even in THF-d_8. The enantioselectivity observed with ligand **10** was similar to the previously reported[13]. The results show that β-aminoalcohols provide much better enantioselectivities than the ligands synthesized[1,2].

Table 1. ^{13}C NMR chemical shifts of compounds **8–17** ($CDCl_3$, δ in *ppm* from TMS; assignments marked with asterisks are tentative; for the numbering of the C-atoms, see Scheme 1)

C-atom No.	8	9	10	11	12	13	14	15	16a	16b	17
1	51.49	54.61	53.45	56.11	56.11	52.44	53.60	51.76	53.46	52.81	53.94
2	78.95	87.22	82.63	129.64	131.39	79.03	86.51	83.59	83.54	n.o.	83.73
3	45.73	47.05	44.23	131.64	131.78	44.06	46.48	45.94	45.22	46.08	45.34
4	44.44	45.47	45.35	51.85	51.92	50.42	49.31	48.85	50.29	49.81	50.88
5	26.47	26.76	26.97	25.81	25.83	25.00	23.95	24.36	25.08	24.84	25.07
6	29.92	30.85	30.69	31.79	31.92	30.63	33.48	32.51	31.68	31.15	32.38
7	48.75	50.69	50.49	55.43	55.51	40.87	42.04	41.98	40.57	41.56	40.49
8	21.08	21.86	21.32	19.75	19.81	27.85	29.68	29.19	28.22	26.18	28.00
9	20.49	21.86	21.16	19.75	19.81	23.15	21.95	22.24	22.73	25.08	22.84
10	10.44	11.26	9.92	12.84	13.03	17.83	17.99	17.11	18.11	15.14	18.47
11	37.09	139.94	163.54	140.32	140.54	35.71	140.23	162.26	135.03	130.88	134.61
12	21.68	129.26*	121.55*	106.93*	107.13	23.56	130.10*	123.09*	105.28*	106.27*	107.63
13	59.90	127.55*	135.51*	107.48*	107.13	61.66	126.70*	134.97*	109.34*	109.86*	107.63
14	-	124.82*	120.57*	122.91	140.54	-	124.39*	121.34*	122.51	123.95	134.61
15	-	123.74*	147.34	-	-	-	123.47*	146.66*	-		-
16	-	153.61	-	-	-	-	152.74	-	-		-
N-CH_3	44.20	48.50 46.33	-	34.99	34.08	45.37	46.99	-	37.56	37.11	36.32

Table 2. Addition of diethylzinc to benzaldehyde catalyzed by aminoalcohols **8–10** and **13–17**

Entry	Catalyst	Solvent[a]	Reaction Temp. [°C]	Reaction Time [h]	Yield[b] [%]	Optical Purity [%][c]
1	**8**	Toluene	r.t.	27	99	56 (*S*)
2	**9**	Toluene	r.t.	1	99	38 (*R*)
3	**9**	Tol./Hex.	0	37	99	41 (*R*)
4	**9**	Tol./Hex.	-20	40	99	42 (*R*)
5	**10**	Tol./Hex.	r.t.	38	99	41 (*R*)
6	**13**	Toluene	r.t.	27	99	58 (*R*)
7	**14**	Tol./Hex.	r.t.	24	99	64 (*R*)
8	**15**	Tol./Hex.	r.t.	50	99	0
9	**16**	Tol./Hex.	r.t.	40	55	10 (*R*)
10	**17**	Tol./Hex.	r.t.	100	80	15 (*S*)

[a] The ratio toluene/hexane was 2/1 (v/v). [b] Yields of isolated 1-phenyl-1-propanol (after Kugelrohr distillation or column chromatography). [c] Determined by polarimetry based on the maximum values described for the specific rotations of *S*-(-)- and *R*-(+)-1-phenyl-1-propanol[14].

However, it is important to note that ligands **8** and **13** (*exo*-OH *vs. endo*-OH) give predominantly (*S*)- and (*R*)-1-phenyl-1-propanol, respectively, indicating a potential possibility to direct the asymmetric induction. The same tendency was observed by *Noyori*[1a] with ligands (1*R*,2*S*)-DAIB (*exo*-OH) and (1*R*,2*R*)-DAIB (*endo*-OH).

In conclusion, we have demonstrated that (+)-camphor and (−)-fenchone can be easily converted into optically active aminoalcohols *via* reactions with suitable organolithium compounds. Further investigations concerning the synthesis of new ligands, providing better enantioselectivities, as well as, additions with other organozincs and aldehydes are in progress.

Experimental section

General methods

All reactions were carried out in flame-dried *Schlenk* flasks under argon atmosphere. THF was distilled over sodium/benzophenone. Hexane was distilled over Na[Et_4Al]. Thin layer chromatography (TLC): aluminium sheets precoated with silica gel 60 F_{254} (Merck). Column chromatography: at normal pressure, silica gel 60 (0.040–0.063 mm, Merck). Melting points (uncorrected): Kofler-block apparatus. $[\alpha]_D^{20}$: Perkin–Elmer 241 polarimeter. Mass spectra (MS): Jeol-JMS-D-300 spectrometer; fragmentation in *m/z* with relative intensities (%) in parentheses. NMR spectra: Bruker Avance DRX-250 (^1H at 250.1 MHz; ^{13}C at 62.9 MHz; TMS as internal standard). Elemental analyses were performed by the Microanalytical Service Laboratory of the Institute of Organic Chemistry.

Starting materials

The following starting materials were used: (1*R*)-(+)-camphor (Fluka AG), (1*R*)-(−)-fenchone (Fluka AG), N,N-dimethylaminopropyl-lithium[7], 2-N,N-dimethylaminophenyl-lithium[8], N-methylpyrrol-2-yl-lithium[8], N-methylpyrrol-2,5-diyl-lithium[9], 2-pyridyl-lithium[8], anhydrous $CeCl_3$[6].

General procedure (GP)

Addition of organolithium reagents **3–7** to camphor **1** and fenchone **2**: The pure ketone **1** or **2** was mixed with $CeCl_3$ in THF and stirred at room temperature for 40 min during which a gel-like mixture (usually slightly yellow coloured) was formed. The organometallic reagents were added rapidly, in the course of which the heterogeneous mixture turned to a deep coloured solution and the temperature rises up to 35–40°C. After stirring for 1–1.5 h the mixture was worked up.

*(1*R,2R*)-2-*exo*-Hydroxy-2-*endo*-(N,N-dimethylaminopropyl)-1,7,7-trimethylbicyclo[2.2.1]heptane 8*

Following **GP**, **8** was prepared from 1.59 g (10.45 mmol) camphor, 2.58 g (10.47 mmol) $CeCl_3$ and 1.35 g (10.50 mmol) of reagent **3**. After 1 h stirring the mixture was hydrolysed with 2 N HCl and extracted with pentane. The acidic aqueous layer was treated with conc. Na_2CO_3 solution, extracted with Et_2O and the ether phase was dried (Na_2SO_4). After evaporation of the solvent the crude product was sublimed in a Kugelrohr apparatus (70°C/0.001 Torr) to give 1.93 g (77%) of **8** as colourless crystalline solid. mp 38–40°C. $[\alpha]_D^{20}$= −3.29 (c 4.07, $CHCl_3$). Anal. calc. for $C_{15}H_{29}NO$ (239.4): C, 75.26; H, 12.21; N, 5.85; found: C, 75.20; H, 12.16; N, 5.97. MS (EI) *m/z* (rel. int.): 239 (M^+, 9). ^1H NMR ($CDCl_3$, 300 K): δ=0.84 (s, 3H, H-9), 0.87 (s, 3H, H-10), 0.92–1.02 (m, 1H, H-5_{endo}), 1.12 (s, 3H, H-8), 1.31–1.43 (m, 3H, H-3_{endo}, H-6_{exo}, H-6_{endo}), 1.58–1.72 (m, 6H, H-4, H-5_{exo}, H-11, H-12), 1.95 (dt, 1H, H-3_{exo}, J=12.7, 3.7 Hz), 2.22 (s, 6H, N–CH_3), 2.25–2.31 (m, 2H, H-13), 4.32 (s, 1H, OH).

*(1*R,2R*)-2-*endo*-Hydroxy-2-*exo*-(N,N-dimethylaminopropyl)-1,3,3-trimethylbicyclo[2.2.1]heptane 13*

Following **GP**, **13** was prepared from 1.75 g (11.50 mmol) fenchone, 2.83 g (11.48 mmol) $CeCl_3$ and 1.49 g (11.59 mmol) of reagent **3**. After 1 h stirring the mixture was hydrolysed with 2 N HCl and extracted with pentane. The acidic aqueous layer was treated with conc. Na_2CO_3 solution, extracted with Et_2O and the ether phase was dried (Na_2SO_4). After evaporation of the solvent the crude product was distilled (Kugelrohr 70°C/0.001 Torr) to give 2.67 g (97%) of **13** as oil. $[\alpha]_D^{20}$= −11.93 (c 4.27, $CHCl_3$). Anal. calc. for $C_{15}H_{29}NO$ (239.4): C, 75.26; H, 12.21; N, 5.85; found: C, 75.17; H, 12.09; N, 5.54. MS (EI) *m/z* (rel. int.): 239 (M^+, 8). ^1H NMR ($CDCl_3$, 300 K): δ=0.87–0.94 (m, 1H, H-6_{exo}), 0.96 (s, 3H, H-10), 0.97 (s, 3H, H-9), 1.01–1.06 (m, 1H, H-7_{anti}), 1.31–1.46 (m, 2H, H-5_{exo}, H-11_b), 1.51–1.63 (m, 4H, H-7_{syn}, H-12). 1.66–1.78 (m, 1H, H-5_{endo}), 1.80–1.90 (m, 1H, H-11_a), 2.04–2.17 (m, 1H, H-6_{endo}), 2.19–2.25 (m, 2H, H-13), 2.24 (s, 6H, NCH_3), 5.25 (s, 1H, OH).

*(1*R,2R*)-2-*exo*-Hydroxy-2-*endo*-(N,N-dimethylamino-2-phenyl)-1,7,7-trimethylbicyclo[2.2.1]heptane 9*

Following **GP**, **9** was prepared from 0.34 g (2.23 mmol) camphor, 0.55 g (2.23 mmol) $CeCl_3$ and 0.60 g (2.47 mmol) of reagent **4** (added in solid form). After 1.5 h stirring the mixture was hydrolysed

with 2 N HCl and the unreacted ketone (0.20 g) was extracted with Et_2O. The acidic aqueous layer was treated with conc. Na_2CO_3 solution, extracted with Et_2O and the ether phase was dried (Na_2SO_4). After evaporation of the solvent the crude product was chromatographied (Ø 17 mm, h=490 mm, 42 g silica gel, hexane/Et_2O=5:1) to give 0.046 g (8%) of **9**, 0.006 g (1%) of *m*-dimethylamino product and 0.021 g (4%) of *p*-dimethylamino product, as yellow crystalline solids.

Data for 9: mp 79–81°C. $[\alpha]_D^{20}$= −9.68 (c 2.0, $CHCl_3$). Anal. calc. for $C_{18}H_{27}NO$ (273.4): C, 79.07; H, 9.95; N, 5.12; found: C, 79.03; H, 9.89; N, 5.38. MS (CI) *m/z* (rel. int.): 274 ($[M+1]^+$, 100). ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.88 (s, 3H, H-9), 0.71 (s, 3H, H-10), 1.27 (s, 3H, H-8), 1.03 (m, 1H, H-5_{endo}), 1.18–1.40 (m, 2H, H-6), 1.73–1.80 (m, 1H, H-5_{exo}), 1.86 (t, 1H, H-4, J=6.6 Hz), 2.16 (d, 1H, H-3_{endo}, J=14 Hz), 2.28 (dt, 1H, H-3_{exo}, J=14.0, 4.0 Hz), 2.63 (s, 3H, H–NCH_3), 2.74 (s, 3H, H–NCH_3), 7.12–7.38 (m, 4H, H–Ph), 9.40 (s, 1H, OH).

*(1*R,2R*)-2-*endo-*Hydroxy-2-*exo-*(N,N-dimethylamino-2-phenyl)-1,3,3-trimethylbicyclo[2.2.1]heptane* ***14***

Following **GP**, **14** was prepared from 0.32 g (2.10 mmol) fenchone, 0.52 g (2.11 mmol) $CeCl_3$ and 0.57 g (2.34 mmol) of reagent **4** (added in solid form). After 1.5 h stirring the mixture was hydrolysed with 2 N HCl, and the unreacted ketone (0.22 g) was extracted with Et_2O. The acidic aqueous layer was treated with conc. Na_2CO_3 solution, extracted with Et_2O and the ether phase was dried (Na_2SO_4). After evaporation of the solvent the crude product was chromatographied (Ø 17 mm, h=490 mm, 44 g silica gel, hexane/Et_2O=6:1) to give 0.025 g (4%) of **14**, 0.053 g (9%) of *m*-dimethylamino product and 0.031 g (6%) of *p*-dimethylamino product, as yellow crystalline solids.

Data for 14: mp 57–60°C. $[\alpha]_D^{20}$= −49.54 (c 2.0, $CHCl_3$). Anal. calc. for $C_{18}H_{27}NO$ (273.4): C, 79.07; H, 9.95; N, 5.12; found: C, 79.03; H, 9.89; N, 5.34. MS (EI) *m/z* (rel. int.): 273 (M^+, 14). ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.47 (s, 3H, H-9), 1.02–1.15 (m, 1H, H-6_{exo}), 1.11 (s, 3H, H-8), 1.15 (s, 3H, H-10), 1.32 (dd, 1H, H-7_{anti}, J=10.4, 1.5 Hz), 1.36–1.48 (m, 1H, H-5_{exo}), 1.73–1.84 (m, 2H, H-5_{endo}), 2.31 (dq, 1H, H-7_{syn}, J=10.4, 2.2 Hz), 2.36–2.47 (m, 1H, H-6_{endo}), 2.66 (s, 3H, H–NCH_3), 2.68 (s, 3H, H–NCH_3), 7.09–7.23 (m, 2H, H–Ph), 7.31–7.35 (m, 1H, H–Ph), 7.54–7.58 (m, 1H, H–Ph), 9.75 (s, 1H, OH).

*(1*R,2R*)-2-*exo-*Hydroxy-2-*endo-*(2-pyridyl)-1.7.7-trimethylbicyclo[2.2.1]heptane* ***10***

Following **GP**, **10** was prepared from 0.45 g (2.96 mmol) camphor, 0.73 g (2.96 mmol) $CeCl_3$ and reagent **5** (synthesised according[8] at −78°C from 0.63 g (4.00 mmol) 2-brompyridine and 3.33 ml 1.32 M solution of n-BuLi in hexane). The addition reaction was carried out at −78°C since the lithium reagent is rather unstable. After 1.5 h stirring at room temperature the reaction mixture was hydrolysed with 2 N HCl and diluted with 50 ml ether. The organic layer was washed with 2 N HCl in order to extract the product as hydrochloride. The acidic aqueous layer was treated with conc. Na_2CO_3 solution, extracted with ether and dried (Na_2SO_4). After evaporation of the solvent the crude product was purified by column chromatography (Ø 13 mm, h=430 mm, 26 g silica gel, hexane/Et_2O=6:1) to give 0.36 g (53%) of **10** (colourless crystals). mp 54–56°C. $[\alpha]_D^{20}$= −34.35 (c 2.0, $CHCl_3$). Anal. calc. for $C_{15}H_{21}ON$ (231.3): C, 77.88; H, 9.15; N, 6.05; found: C, 77.82; H, 9.13; N, 6.29. MS (EI) *m/z* (rel. int): 231 (M^+, 20), ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.81 (s, 3H, H-9), 0.84–0.89 (m, 1H, H-5_{endo}), 0.91 (s, 3H, H-10), 1.27 (s, 3H, H-8), 1.22–1.36 (m, 2H, H-6), 1.73–1.83 (m, 1H, H-5_{exo}), 1.91 (t, 1H, H-4, J=4.4 Hz), 2.00 (d, 1H, H-3_{endo}, J=39.7 Hz), 2.32 (dt, 1H, H-3_{exo}, J=14.0, 3.3 Hz), 5.24 (s, 1H, OH), 7.14–7.26 (m, 1H, H-13), 7.44 (d, 1H, H-12, J=8.0 Hz), 7.62–7.69 (m, 1H, H-14), 8.52–8.55 (m, 1H, H-15).

*(1*R,2R*)-2-*endo-*Hydroxy-2-*exo-*(2-pyridyl)-1.3.3-trimethylbicyclo[2.2.1]heptane* ***15***

Following **GP**, **15** was prepared from 0.45 g (2.96 mmol) camphor, 0.73 g (2.96 mmol) $CeCl_3$ and reagent **5**. (synthesised according[8] at −78°C from 0.63 g (4.00 mmol) 2-Brompyridine and 3.33 ml 1.32 M solution of n-BuLi in hexane). The addition reaction was carried out at −78°C since the lithium reagent is rather unstable. After 1.5 h stirring at room temperature the reaction mixture was

hydrolysed with 2 N HCl and diluted with 50 ml ether. The organic layer was washed with 2 N HCl in order to extract the product as hydrochloride. The acidic aqueous layer was treated with conc. Na_2CO_3 solution, extracted with ether and dried (Na_2SO_4). After evaporation of the solvent the crude product was purified by column chromatography (Ø 13 mm, h=430 mm, 26 g silica gel, hexane/Et_2O=7:1) to give 0.45 g (66%) of **15** (colourless crystals). mp 58–60°C. $[\alpha]_D^{20}$= −28.17 (c 2.0, $CHCl_3$). Anal. calc. for $C_{15}H_{21}ON$ (231.3): C, 77.88; H, 9.15; N, 6.05; found: C, 77.97; H, 9.23; N, 6.17. MS (EI) *m/z* (rel. int): 231 (M^+, 10), ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.43 (s, 3H, H-9), 0.98 (s, 3H, H-8), 0.99 (s, 3H, H-10), 1.09–1.20 (m, 1H, H-6$_{exo}$), 1.36 (dd, 1H, H-7$_{anti}$, J=10.5, 1.4 Hz), 1.42–1.55 (m, 1H, H-5$_{exo}$), 1.79–1.92 (m, 2H, H-5$_{endo}$), 2.24–2.40 (m, 2H, H-6$_{endo}$, H-7$_{syn}$), 5.80 (s, 1H, OH), 7.12–7.17 (m, 1H, H-13), 7.52 (d, 1H, H-12, J=8.0 Hz), 7.60–7.67 (m, 1H, H-14), 8.47–8.50 (m, 1H, H-15).

*(1*R*)-2-(1-Methyl-pyrrol-2-yl)-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene* ***11***

Following **GP**, **11** was prepared from 0.51 g (3.35 mmol) camphor, 0.83 g (3.37 mmol) $CeCl_3$ and 7.08 ml 0.71 M THF solution of reagent **6**. After 1.5 h stirring the reaction mixture was hydrolysed with 2 N HCl, extracted with ether washed with water and dried ($NaSO_4$). After evaporation of the solvent the crude product was chromatographied (Ø 24 mm, h=520 mm, 85 g silica gel, hexane/Et_2O=7:1) to give 0.53 g (74%) of **11** as orange oil. $[\alpha]_D^{20}$= −90.04 (c 2.0, $CHCl_3$). Anal. calc for $C_{15}H_{21}N$ (215.3): C, 83.67; H, 9.83; N, 6.50; found: C, 83.75; H, 9.76; N, 6.71. MS (CI) *m/z* (rel. int): 216 ($[M+1]^+$, 100). ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.82 (s, 3H, H-9), 0.90 (s, 3H, H-8), 1.09 (s, 3H, H-10), 1.01–1.26 (m, 2H, H-6$_{endo}$, H-5$_{endo}$), 1.55–1.65 (m, 1H, H-6$_{exo}$), 1.88–1.97 (m, 1H, H-5$_{exo}$), 2.42 (t, 1H, H-4, J=3.5 Hz), 3.59 (s, 3H, H-15), 5.86 (d, 1H, H-3, J=3.3 Hz), 6.03 (dd, 1H, H-12, J=3.6, 1.7 Hz), 6.11 (dt, 1H, H-13, J=3.6, 1.7 Hz), 6.61 (t, 1H, H-14, J=2.5 Hz).

*(1*R*,2*R*)-2-*endo*-Hydroxy-2-*exo*-(1-methylpyrrol-2-yl)-1,3,3-trimethyl-bicyclo[2.2.1]heptane* ***16***

Following **GP**, **16** was prepared from 0.69 g (4.53 mmol) fenchone, 1.12 g (4.54 mmol) $CeCl_3$ and 9.57 ml 0.71 M THF solution of reagent **6**. After 1.5 h stirring the reaction mixture was hydrolysed with 2 N HCl, extracted with ether washed with water and dried ($NaSO_4$). After evaporation of the solvent the crude product was chromatographied (Ø 24 mm, h=520 mm, 85 g silica gel, hexane/Et_2O=10:1) to give 0.75 g (71%) of **16** as orange oil. $[\alpha]_D^{20}$= −38.27 (c 2.0, $CHCl_3$). Anal. calc for $C_{15}H_{23}NO$ (233.4): C, 77.21; H, 9.93; N, 6.00; found: C, 77.28; H, 9.79; N, 5.86. MS (CI) *m/z* (rel. int): 234 ($[M+1]^+$, 100). ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.54 (s, 3H, H-9), 1.13 (s, 3H, H-8), 1.09–1.27 (m, 2H, H-6$_{exo}$, H-7$_{anti}$), 1.27 (s, 3H, H-10), 1.33–1.47 (m, 1H, H-5$_{exo}$), 1.66–1.77 (m, 2H, H-5$_{endo}$, H-4), 2.07–2.19 (m, 1H, H-6$_{endo}$), 2.31 (dq, 1H, H-7$_{syn}$, J=10, 2.2 Hz), 3.78 (s, 3H, H-15), 6.00 (q, 1H, H-13, J=3.8, 1.7 Hz), 6.13 (q, 1H, H-12, J=3.8, 1.7 Hz), 6.46 (t, 1H, H-14, J=1.9 Hz).

*1-Methyl-2,5-bis[(1*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl]-pyrrol* ***12***

Following **GP**, **12** was prepared from 0.86 g (5.65 mmol) camphor, 1.39 (5.64 mmol) $CeCl_3$ and 0.59 g (2.82 mmol) of reagent **7**. After 1.5 h stirring the reaction mixture was hydrolysed with 2 N HCl, extracted with ether and dried (Na_2SO_4). After evaporation of the solvent the crude product was chromatographied (Ø 17 mm, h=490 mm, 44 g silica gel, hexane/Et_2O=30:1) to give 0.05 g (5%) of **12** (colourless crystalline solid), 0.40 g (32%) of **11** and 0.42 g unreacted camphor.

Data for 12: mp 128–130°C. $[\alpha]_D^{20}$= −47.64 (c 0.9, $CHCl_3$). Anal. calc. for $C_{25}H_{35}N$ (349.56): C, 85.90; H, 10.09; calc. C, 86.93; H, 10.66. ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.82 (s, 6H, H-9), 0.90 (s, 6H, H-8), 1.12 (s, 6H, H-10), 1.03–1.27 (m, 4H, H-6$_{endo}$, H-5$_{endo}$), 1.55–1.64 (m, 2H, H-6$_{exo}$), 1.88–1.99 (m, 2H, H-5$_{exo}$), 2.42 (t, 2H, H-4, J=3.4 Hz), 3.52 (s, 3H, H-15), 5.88 (d, 2H, H-3, J=3.4 Hz), 6.03 (s, 2H, H-12, H-13)

*1-Methyl-2,5-bis[(1*R*,2*R*)-2-*endo*-Hydroxy-1,3,3-trimethylbicyclo[2.2.1]hept-2-yl]-pyrrol* ***17***

Following **GP**, **17** was prepared from 1.16 g (7.62 mmol) fenchone, 1.88 g (7.63 mmol) $CeCl_3$ and 0.80 g (3.82 mmol) of reagent **7**. After 1.5 h stirring the reaction mixture was hydrolysed with 2 N HCl, extracted with ether, washed with water and dried (Na_2SO_4). After evaporation of the solvent

the crude product was chromatographied (Ø 24 mm, h=520 mm, 85 g silica gel, hexane/Et_2O=25:1) to give 0.10 g (10%) of **17** (colourless crystalline solid), 0.47 g (26%) of **16** and 0.70 g unreacted fenchone.

Data for 17: mp 130–133°C. $[\alpha]_D^{20}$= −31.33 (c 1.5, $CHCl_3$). Anal. calc. for $C_{24}H_{39}O_2N$ (373.6): C, 77.16; H, 10.52; found: C, 77.25; H, 10.35. ^{1}H-NMR ($CDCl_3$, 300 K): δ=0.53 (s, 6H, H-9), 1.12 (s, 6H, H-8), 1.07–1.25 (m, 4H, H-6_{exo}, H-7_{anti}), 1.29 (s, 6H, H-10), 1.31–1.40 (m, 2H, H-5_{exo}), 1.63–1.74 (m, 4H, H-5_{endo}, H-4), 2.10–2.22 (m, 2H, H-6_{endo}), 2.33 (dq, 2H, H-7_{syn}, J=10.2, 2.2 Hz), 3.95 (s, 3H, H-15), 6.00 (s, 2H, H-12, H-13).

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13. All data published for **10** in ref.[4] are corresponding to those obtained now using (+)-1*R*-camphor, however the formula given in ref.[4] is somewhat confusing, showing an absolute configuration 1*S* for the camphor skeleton.
14. (a) Fluka-Catalogue 1995/96, p. 1185, for the (*S*)-(−)-isomer $[\alpha]_D^{20}$= −47 (c=2.2, hexane) and for the (*R*)−(+)-isomer $[\alpha]_D^{20}$=+47 (c=2.2, hexane). (b) Ref.[2d] for the (*S*)-(−)-isomer $[\alpha]_D^{20}$= −47.6 (c=6.11,$CHCl_3$) and for the (*R*)-(+)-isomer $[\alpha]_D^{20}$=+45.4 (c=2.0, EtOH).

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