Pergamon

Tetrahedron Vol. 51, No. 48, pp. 13261-13270, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00849-7

3-*exo*,3'-*exo*-(1*R*,1'*R*)-Bithiocamphor – a Versatile Source for Functionally Different 3,3'-Bibornane Derivatives, II.[1] An Access to 3-*exo*,3'-*exo*-(1*R*,1'*R*)-Bicamphor and Related Compounds☆

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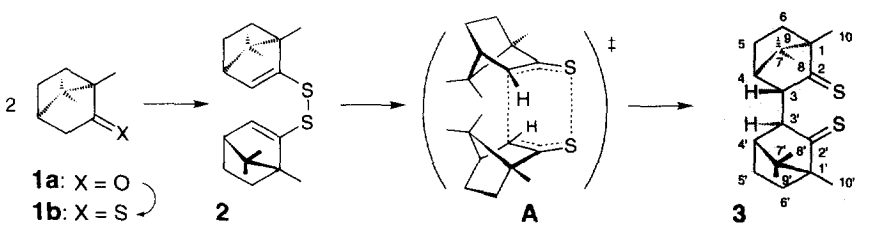
Dedicated to Professor Hans Suschitzky on the occasion of his 80th birthday

Abstract: 3-*exo*,3'-*exo*-(1*R*,1'*R*)-bicamphor (**12**) is obtained from 3-*exo*,3'-*exo*-(1*R*,1'*R*)-bithiocamphor (**3**) by condensation with hydrazine hydrate followed by hydrolysis of the resulting dihydropyridazine **11**. Deprotonation of **12** with NaH and subsequent treatment with potassium hexacyanoferrate(III) furnishes the 2,2'-dioxo-3,3'-bibornanylidene **13**, whilst reduction of **12** with $LiAlH_4$ affords the 3,3'-bi*iso*borneol **16**. Further related transformations to various 2,2'-difunctional 3,3'-bibornane derivatives are described, which are could be of interest as chiral ligands

Introduction

3-*exo*,3'-*exo*-(1*R*,1'*R*)-Bithiocamphor (**3**) is a synthetically useful compound for the access to various 3,3'-bibornane derivatives (*Scheme 1*). The synthetic route to **3** was reported[2] many years ago and involves C,C-bond formation between two (1*R*)-thiocamphor molecules **1b** [derived from (+)-camphor]. The sequence involves deprotonation followed by oxidation to the disulfide **2**, and *Cope* rearrangement of the latter. The transition state of the last step gives rise to the stereospecific formation of the 3-*exo*,3'-*exo* linkage.



Scheme 1

In part I of this series[1] we described various transformations which lead to loss of chirality at C-3 and C-3' by S,S'-ring-closure reactions and by 1,5-protropic rearrangements. We now report a series of reactions with retention of the chirality at C-3 and C-3', especially those involving sulfur-oxygen exchange and reduction of the functional groups. In this connection the ability of **3** to react with hydrazine and with hydroxylamine at the thiocarbonyl groups, as previously described,[2] should be noted.

Results and Discussion

1. Attempts to exchange Sulfur for Oxygen; Access to 3-*exo*,3'-*exo*-(1*R*,1'*R*)-Bicamphor

Several of these attempts failed or resulted in product mixtures containing frequently the diborneno-anellated thiophene **4** and 1,2,3-trithiepine **10**, obviously due to steric hindrance or to the proximity of the two thiocarbonyl groups,[3] respectively (*Scheme 2*). The high tendency for the formation of these components has been already outlined in our previous paper.[1]

Thus, reaction of mercury(II) acetate on **3** affords the thiophene **4**, whilst similar treatment of the monothione **5**, obtained as described in ref.[1], smoothly produces the bornylidene-camphor **6**. From the reaction of **3** with $NaNO_2$ in aqueous HCl solution at elevated temperature, according to ref.[4], the intense green coloured oxo-thioxo-bibornylidene **9** (λ_{max} = 635 nm) is formed in low yield along with **4** and **10**. The (*E*)-configuration of **9** is established by X-ray analysis (*Figure 1*)[5a,c] and its formation can be explained by isomerization of **3** to **7** and **8** under the acidic conditions as previously stated in ref.[1].

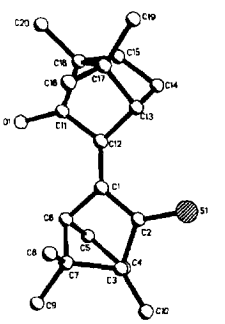
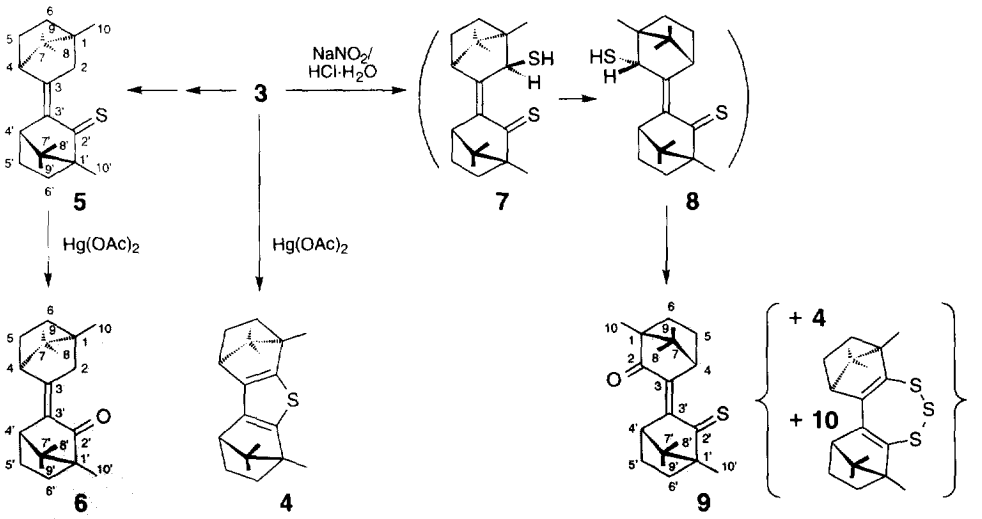


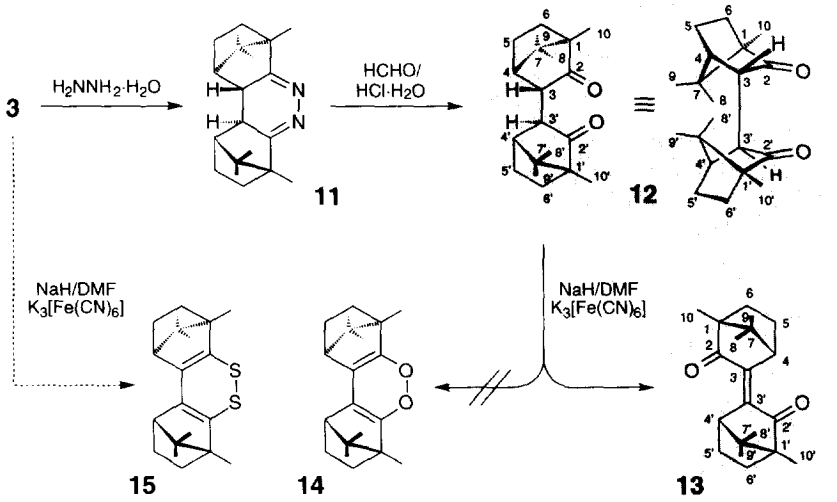
Figure 1. X-ray crystal structure[5a,c] of 2-oxo-2'-thioxo-(*E*)-3,3'-bibornanylidene (**9**).
Caused by disorder in the crystal, the C-S- and C-O-bond lengths appear almost equal [1.505(8) and 1.522(9) Å, respectively].



Scheme 2

The conversion of both thioxo groups in **3** to oxo groups with conservation of the 3-*exo*,3'-*exo*-linkage requires techniques that avoid the intramolecular interchange of both thioxo groups as well as any competing isomerization via **7** and **8** in the primary steps, respectively. Such an approach (*Scheme 3*) can be achieved by the conversion of **3** to the dihydropyridazine **11** by the action of hydrazine hydrate as described in ref.[2a]. From NMR the 3-*exo*,3'-*exo*-linkage in **11** is preserved (singlets of the H-3 and H-3' signals, ten ^{13}C-NMR signals and nine ^{1}H-NMR signals indicating the equivalence of both bornane units). The intermediate **11** can be readily hydrolyzed by dilute hydrochloric acid and formaldehyde solution under reflux, leading smoothly to the 3,3'-bicamphor **12** in good yield. Here also the *exo*,*exo*-linkage of both camphor units is preserved as confirmed by

NMR [no coupling between H-3 or H-3' and H-4 or H-4', respectively (dihedral angle H-3/H-4 ≈ 90°), doublet for H-4 due to coupling with H-5$_{exo}$, $^3J_{4,5exo}$ = 4.7 Hz]. This result points to a remarkable resistance of **12** towards enolization in the acidic medium (cf. the deviating behaviour of the sulfur analogous **3** in ref.[1]). By contrast, it has been shown that in alkaline conditions isomerization of **12** occurs producing its *endo,endo*-isomer as the most stable one.[6]



Scheme 3

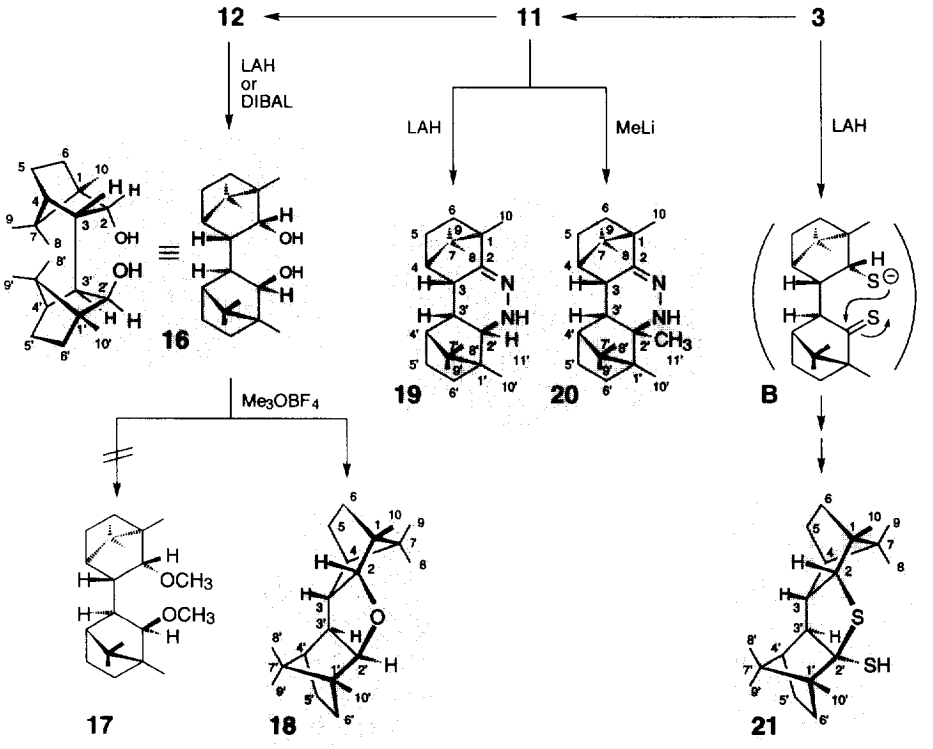
Despite the circuitous route from **1a** via **1b** → **2** → **3** to **12**, this sterically homogeneous method to **12** should be of advantage compared with other methods so far described[7]. In these, the direct C-C-bond formation using camphor or 3-bromocamphor leads predominatly to mixtures of the stereoisomers, whereas in our method the *Cope*-rearrangement of **2** to **3** serves as the sterically controlling key step. All attempts to simplify the route to **12** by an analogous transformation starting from (1*R*)-(+)-camphor azine[8] failed, despite numerous variations of the reaction conditions (e.g. action of acids, alkylation, acylation, deprotonation with the aid of e.g. *sec*-BuLi or LDA).[9]

The oxidation of **12** under the same conditions used for the oxidation of **3** to the 1,2-dithiine **15** again reinforces the complete difference between the behaviour between the oxygen and the sulfur series: Treatment of **12** with sodium hydride in DMF followed by the addition of potassium hexacyanoferrate(III) leads to the dioxobibornylidene **13** rather than to the 1,2-dioxine **14**.[10] The assigned (*E*)-configuration is in accord with the IR and Raman spectra (rule of mutual exclusion due to the C_2-symmetry of the endione substructure (i.e. a strong C=O and no C=C absorption in the IR and conversely a very weak C=O- and a strong C=C-absorption in the Raman spectrum). Further evidence includes the very low-field shift of the H-4 (H-4') NMR signal at 3.70 ppm (cf. **6** and **9**).

2. Reduction of the Funtional Groups

These transformations offer an approach to 2,2'-difunctional 3,3'-bibornane derivatives as synthetically interesting chiral ligands. Some preliminary results are presented in *Scheme 4*. The reduction of **12** with lithiumaluminium hydride or diisobutylaluminium hydride (no significant difference between the effectiveness of either reagent) affords the bi*iso*borneol **16** as main product in addition to its stereoisomers in minor amounts. The alcohol **16** is readily sublimed and may be purified by simple recrystallization from hexane/benzene. Its structure

is elucidated from the following NMR data: Only ten ^{13}C-NMR signals and eleven ^{1}H-NMR signals characterize the equivalence of both bornane rings; they are *exo-exo*-linked because H-3$_{endo}$ does not couple with H-4$_{endo}$, the latter shows only one coupling with H-5$_{exo}$ ($^{3}J_{4,5exo}$ = 4 Hz); the strong NOE between H-2 and H-3 agrees in the best way with their *endo*-position, hence, *exo*-arrangement of the OH-groups. Consequently, hydride attack must occur preferentially at the *endo*-side.



Scheme 4

Surprisingly, the methylation of both OH-groups in **16** proves to be problematic. For example, treatment of **16** with sodium hydride in THF and subsequently with either methyl iodide or dimethyl sulfate leads to incomplete methylation even in the presence of excess reagents (mixture of products including starting material), and the dimethyl ether **17** could not be obtained. On the other hand, the reaction of **16** with trimethyloxonium tetrafluoroborate in dichloromethane proceeds with loss of one of the OH groups and the formation of the tetrahydrofuran **18** (clearly by dimethylation at one of the OH groups, formation of an oxonium ion and elimination). The close similarity of the ^{1}H- and ^{13}C-NMR spectra with those of **16** strongly suggests a structural analogy, e.g. the absence of any coupling between H-3 and H-4 indicates the *endo*-position of H-3 (H-3') as is required for the *cis*-anellation of the bornene units.

The preferential attack at the *endo*-side as noted above should be inevitable then in the case of cyclic compounds as **11**. Treatment of the latter with lithiumaluminium hydride leads predominantly to the mono-reduced compound **19**, despite the use of excess reagents (di-addition is obviously difficult due to charge adjacency). Here also the new H-2' arrives at the same *endo*-position as H-2' in agreement with NMR observations (NOE between H-2'$_{endo}$ and H-3'$_{endo}$ as well as H-3'$_{endo}$ and H-6'$_{endo}$). Analogously, the addition of methyllithium

leads to **20** with an *endo*-orientation of the introduced methyl group in accord with NMR data (NOE between H-3'$_{endo}$ and new CH_3). Nevertheless, this structure is clearly established by X-ray crystallography (*Figure 2*).[5b,c]

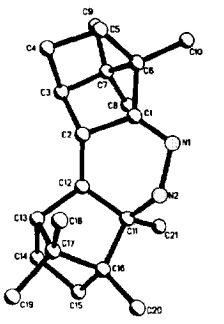


Figure 2. X-ray crystal structure[5b,c] of 6-(*endo*-methyl)-Δ^2-tetrahydro-(1*R*,1'*R*)-diborn-2-eno[2,3-c;3',2'-*e*]pyridazine (**20**).
Selected data – bond lengths: C1-N1 = 1.271(4) Å, C11-N2 = 1.502(5) Å, N1-N2 = 1.431(4) Å.

Unexpectedly, reduction of the starting material **3** with lithiumaluminium hydride leads to the mercaptotetrahydrothiophene **21**. Here the initially produced reduction product **B** suffers from a proximity effect with the attack of the thiolate anion at the remaining thioxo group and thus prevents further attack by the reagent. The structure is supported by all the NMR data (see experimental part).

Conclusions

3-*exo*,3'-*exo*-(1*R*,1'*R*)-Bithiocamphor **3**, obtained from (+)-camphor, serves as a versatile intermediate for the synthesis of various 2,2'-difunctional 3,3'-bibornane derivatives. Whilst the direct exchange of sulfur for oxygen is handicapped by the proximity of the both sulfur atoms (competing formation of the thiophene **4** and the 1,2,3-trithiepine **10**), the desired compound 3-*exo*,3'-*exo*-(1*R*,1'*R*)-bicamphor **12** can be obtained from **3** by reaction with hydrazine hydrate followed by the hydrolysis of the resulting dihydropyridazine **11**. After deprotonation, **12** is oxidized to the dioxo-bibornanylidene **13**, thus demonstrating a complete contrast with the sulfur analogue **3** (which leads to the 1,2-dithiine derivative **15**). Reduction of the functional groups at the 2- and 2'-positions permits ready access to synthetically interesting bidendate chiral ligands. Treatment of **12** with $LiAlH_4$ furnishes the bi*iso*borneol **16**, which cyclizes to the tetrahydrofuran derivative **18** on reaction with Me_3OBF_4. Preferential *endo*-attack is observed in the formation of the tetrahydropyridazine derivatives **19** and **20**, produced from **11** by reduction and by the addition of MeLi respectively. By contrast, reduction of the sulfur counterpart **3** with $LiAlH_4$ affords the tetrahydrothiophene derivative **21** due to the proximity effect which enables the initially formed SH group to add intramolecularly to the remaining C=S group.

Acknowledgements: The authors are indebted to the Fonds der Chemischen Industrie, Frankfurt/Main, and the Deutsche Forschungsgemeinschaft for financial support. The editorial assistance by Dr. A. Dunn, Frankfurt/-Main, is gratefully acknowledged.

Experimental Part

NMR spectra:Varian Unity 500 (^{1}H: 499.84 MHz, ^{13}C: 125.71 MHz), Bruker WP 200 (^{1}H: 200.13 MHz, ^{13}C: 50.3327 MHz), Bruker AC 80 (^{1}H: 80.13 MHz, ^{13}C: 20.149 MHz). ^{1}H- and ^{13}C-NMR spectra were recorded with TMS as internal standard. – MS: Varian MAT CH6, AMD Intectra 402 (70 eV). – IR: Carl Zeiss Jena Specord 71 and 75. – UV: Beckman DK-2A. – Column chromatography (CC): silica gel [60 mesh (Merck)]. – Optical rotations: Polarimeter 241 (Perkin Elmer), Polartronic (Schmidt & Haensch). – HPLC: Merck Hitachi L-4000 (UV detector). – Melting points: Heating stage microscope (Boetius M; all temperatures quoted are not corrected). – X-ray analyses: Diffractometer STADI4 (Stoe, MoK_α radiation, $3 < 2\Theta < 54°$). – Elemental analyses: Carlo Erba (automatic apparatus).

(1*R*,1'*R*)-3-*exo*,3'-*exo*-Bithiocamphor (**3**). – Preparation according to ref.[2c]; further characteristics: ref.[1a].

2-Oxo-(1*R*,1'*R*)-(*Z*)-3,3'-bibornanylidene (**6**). – A mixture of 302 mg (1 mmol) **5**[1a], 30 ml CH_2Cl_2, 10 ml AcOH, and 1 g (3 mmol) $Hg(OAc)_2$ (immediate change from dark violet to brown-yellow) is refluxed under stirring during 1 h. The residue after evaporation of the solvent is recrystallized from 70-perc. EtOH in the

presence of some activated carbon. – Colourless leaflets; yield: 200 mg (70%); m.p. 96-97°C. – IR (nujol): $\tilde{\nu}$ = 1700 cm^{-1} (s, C=O). – UV/Vis (MeCN): λ_{max} (lg ε): 252 nm (4.56). – $[\alpha]_D^{20}$ = +278° ($CHCl_3$, c = 1, d = 1 cm). – ^1H NMR ($CDCl_3$)[11a]: δ = 0.76, 0.78, 0.89, 0.91, 0.92, 0.93 (18 H, 6 CH_3), 1.18 (H-5*endo*), 1.26 (H-6*endo*), 1.30 (H-5'endo), 1,35 (H-6'*endo*), 1.59 (H-6*exo*), 1.62 (H-6'*exo*), 1.89 (H-5*exo*), 1.97 (H-5'*exo*), 2.29 (H-4), 2.37 (H-2*endo*), 2.53 (H-4'), 2.53 (H-2*exo*); $^3J_{4',5'exo}$ = 3.8 Hz, $^3J_{4,5exo}$ = 4.4 Hz, $^4J_{2exo,6exo}$ = 3.5 Hz, $^2J_{2endo,2exo}$ = 18.6 Hz. – ^{13}C NMR ($CDCl_3$)[11a]: δ = 9.3, 15.0, 18.1, 18.6, 19.5, 20.4 (6 CH_3), 25.6 (C-5), 26.9 (C-5'), 30.3 (C-6'), 35.0 (C-6), 44.1 (C-2), 45.9, 46.6, 47.3 (C-1, C-7, C-7'), 49.3 (C-4'), 53.2 (C-4), 58.2 (C-1'), 131.6 (C-3), 154.1 (C-3'), 208.2 (C-2'). – MS (70 eV), *m/z* (%): 286 (100) [M^+], 271 (25) [$M^+ - CH_3$], 243 (40) [$M^+ - C_3H_7$]. – $C_{20}H_{30}O$ (286.4): calcd. C 83.86, H 10.56; found C 83.44, H 10.29.

2-Oxo-2'-thioxo-(*E*)-3,3'-bibornanylidene (**9**). – A solution of 345 mg (5 mmol) $NaNO_2$ in 10 ml water is added drowise to a stirred solution of 668 mg (2 mmol) **3** in a mixture of 40 ml CH_2Cl_2 and 10 ml concd. HCl at 45°C. After the addition the mixture is heated under reflux for 5 h (bath temperature 60°C). The oily residue after evaporation of the solvent is purified by CC [*n*-hexane/C_6H_6 (4:1)]: 1st fraction (yellow, 100 mg) contains **4** and **10**; 2nd fraction [green, 68 mg (12%)] contains **9**, recrystallization from EtOH/H_2O (6:1). – Green needles; m.p. 141-142°C. – IR (2-perc. $CHCl_3$ solution): $\tilde{\nu}$ = 2930-2850 cm^{-1} (s, C-H), 1710 (s, C=O). – Raman (solid, 200 scans): $\tilde{\nu}$ = 1720 cm^{-1} (w, C=O), 1276 (s, C=S). – UV/Vis (MeCN): λ_{max} (lg ε): 221 nm (4.38), 260 (4.44), 334 (4.56), 635 (4.07). – X-ray analysis in *Figure 1*[5a,c]. – $[\alpha]_D^{20}$ = +174.47° (CH_2Cl_2, c = 2.0 g/100 ml, d = dm). – ^1H NMR ($CDCl_3$)[11a]: δ = 0.74, 0.76, 0.93, 0.97, 1.01, 1.11 (18 H, 6 CH_3), 1.24, 1.27 (H-5*endo*/H-5'*endo*), 1.24, 1.42 (H-6*endo*/H-6'*endo*), 1.69, 1.73 (H-6*exo*/H-6'*exo*), 2.00, 2.08 (H-5*exo*/H-5'*exo*). 4.05, 4.18 (H-4/H-4'), $^3J_{4,5exo}/^3J_{4',5'exo}$ = 4.2/4.3 Hz. – ^{13}C NMR (C_6D_6): δ = 9.6, 13.5, 20.4, 20.7, 25.4, 25.7 (6 CH_3), 18.3, 19.1, 31.4, 35.2 (4 CH_2), 45.7, 48.5, (2 CH), 49.5, 50.5, 58.1, 70.6 (4 C, quatern.), 141.3, 147.5 (2 C, olefin.), 211.9 (C=O), 259.5 (C=S). – MS (70 eV), *m/z* (%): 316 (100) [M^+], 283 (44) [M^+ – SH], 273 (76) [$M^+ - C_3H_7$]. – $C_{20}H_{28}OS$ (316.1): calcd. C 75.90, H 8.86, S 10.12; found C 75.31, 8.83, S 10.10.

4,5-Dihydro-(1*R*,1'*R*)-diborn-2-eno[2,3-*c*;3',2'-*e*]pyridazine (**11**). – Obtained from **3** according to ref.[2a]. – Colourless leaflets; m.p. 208-209°C [from EtOH/H_2O (4:1); ref.[2a]: 200°C dec.]. – ^1H NMR ($CDCl_3$)[11a]: δ = 0.95 (H-9, H-9'), 1,00 (H-8, H-8'), 1.05 (H-10, H-10'), 1.25 (H-5*endo*, H-5'*endo*), 1.59 (H-6*endo*, H-6'*endo*), 1.65 (H-6*exo*, H-6'*exo*), 1.84 (H-4, H-4'), 1.98 (H-5*exo*, H-5'*exo*), 2.09 (H-3*endo*, H-3'*endo*); $^3J_{3,4}$ = 0, $^3J_{4,5exo}$ = 3.9: *exo,exo*-bonding of the bornane units. – ^{13}C NMR ($CDCl_3$)[11a]: δ = 10.3 (C-10, C-10'), 21.6 (C-9, C-9' or C-8, C-8'), 21.8 (C-8, C-8' or C-9, C-9'), 30.0 (C-6, C-6'), 30.7 (C-5, C-5'), 42.1 (C-3, C-3'), 46.0 (C-4, C-4'), 49.1 (C-7, C-7'), 51.5 (C-1, C-1'), 174.6 (C-2, C-2'). – MS (70 eV), *m/z* (%): 298 (62) [M^+], 283 (18) [$M^+ - CH_3$], 270 (9) [$M^+ - N_2$], 258 (13) [$M^+ - 2\ CH_3$], 227 (100) [$M^+ - N_2 - C_3H_7$].

3-*exo*,3'-*exo*-(1*R*,1'*R*)-Bicamphor (**12**). – A suspension of 900 mg **11** in 30 ml aqueous formaldehyde (formalin), 20 ml H_2O and 5 ml concd. HCl is heated under reflux for 4 h. After complete solution achieved, the product continuously precipitates. The product is removed by filtration and recrystallized from 70-perc. EtOH. – Colourless leaflets; yield: 680 mg (75%); m.p. 150-151°C (cf. characteristics under ref.[7]; vacuum sublimation: 100-120°C/10 Torr. – IR (nujol): $\tilde{\nu}$ = 1730 cm^{-1} (s, C=O). – UV (MeCN): λ_{max} (lg ε): 272 nm (2.38). – $[\alpha]_D^{20}$ = +140° (EtOH, c = 1, d = 1 dm). – ^1H NMR ($CDCl_3$)[11a,12]: δ = 0.74 (H-9, H-9'), 0.88 (H-10, H-10'), 0.91 (H-8, H-8'), 1.30 (H-6*endo*, H-6'*endo*), 1.54 (H-5*endo*, H-5'*endo*), 1.62 (H-6exo, H-6'exo), 1.97 (H-5*exo*, H-5'*exo*), 2.02 (H-3*endo*, H-3'*endo*), 2.10 (H-4, H-4'); $^3J_{3,4}$ = 0 (dihedral angle H-3/H-4 ≈ 90°), $^3J_{4,5exo}$ = 4.7: *exo,exo*-bonding of the camphor units (cf. ref.[6,12]), $^2J_{5exo,5endo}$ = -13.1, $^3J_{5exo,6exo}$ = 11.2, $^3J_{5exo,6endo}$ = 3.8, $^3J_{5endo,6endo}$ = 8.8, $^3J_{5endo,6exo}$ = 4.3, $^2J_{6exo,6endo}$ = -13.4. – ^{13}C NMR ($CDCl_3$)[13]: δ = 9.4 (C-10, C-10'), 20.1 (C-8), 21.1 (C-9, C-9'), 28.9 (C-6, C-6'), 29.0 (C-5, C-5'), 46.8 (C-7, C-7'), 46.9 (C-4, C-4'), 54.3 (C-3, C-3'), 57.3 (C-1, C-1'), 219.1 (C-2, C-2'). – MS (70 eV), *m/z* (%): 302 (100) [M^+], 287 (13) [M^+ - CH_3], 274 (68) [M^+ - C_2H_4], 259 (48) [M^+ - C_3H_7]. – $C_{20}H_{30}O_2$ (302.4): calcd. C 79.7, H 9.93; found C 78.91, H 9.99.

2,2'-Dioxo-(*E*)-3,3'-bibornanylidene (**13**). – A solution of 302 mg (1 mmol) **12** in 20 ml anhydrous DMF is added with stirring and under an argon atmosphere to a suspension of 500 mg NaH (16.5 mmol, 80-perc. suspension in paraffin oil) in 5 ml anhydrous DMF at ambient temperature. The mixture is then heated at around 60°C for 7 h. After the addition of 1 g (3 mmol) $K_3[Fe(CN)_6]$ at 40-50°C, stirring is continued for a further hour. The mixture is cooled to 0°C, 30 ml water are added and the precipitated solids removed by filtration. The product is purified by CC ($CHCl_3$), the first yellow fraction affords the product (the second fraction contains some starting material). – Yellow plates (recrystallized from 70-perc. EtOH; vacuum sublimation at 110-130°C/10 Torr); yield: 204 mg (69%); m.p. 144-145°C. – IR (nujol): $\tilde{\nu}$ = 1740 cm^{-1} (s, C=O), absence of bands 1600-1700 (C=C). – Raman (solid, 100 scans): $\tilde{\nu}$ = 1735 cm^{-1} (w, C=O), 1659 (s, C=C). – UV (MeCN): λ_{max} (lg ε): 270 nm (4.01), 330 (1.89). – $[\alpha]_D^{20}$ = +298° ($CHCl_3$, c = 1, d = 1 dm). – ^{1}H NMR ($CDCl_3$)[11a]: δ = 0.74, 0.94, 0.95 (18 H, 6 CH_3), 1.26 (H-5*endo*, H-5'*endo*), 1.38 (H-6*endo*, H-6'*endo*), 1.68 (H-6*exo*, H-6'*exo*), 2.04 (H-5*exo*, H-5'*exo*), 3.71 (H-4, H-4'); $^3J_{4,5exo}$ = 4.4 Hz. – ^{13}C NMR ($CDCl_3$): δ = 9.1, 16.3, 20.7, 25.9, 30.6, 46.0, 48.4, 58.1 (8 C, saturd.), 140.8, (2 C, olefin.), 211.7 (C=O). – MS (70 eV), *m/z* (%): 300 (100) [M^+], 285 (58) [$M^+ - CH_3$], 272 (96) [$M^+ - C_2H_4$], 257 (50) [$M^+ - C_3H_7$]. – $C_{20}H_{28}O_2$ (300.4): calcd. C 80.10, H 9.41; found C 79.84, H 9.57.

3-exo,3'-exo-Bi*iso*borneol (**16**). – A solution of 1.0 g (3.3 mmol) **12** in 70 ml anhydrous diethylether is added with stirring to a suspension of 560 mg (14.85 mmol) $LiAlH_4$ in 50 ml anhydrous diethylether over a 45 minute period . After heating under reflux for 5 h and standing at ambient temperature for 12 h, the mixture is decomposed by the cautious addition of water with ice cooling. The aqueous phase is extracted three times with diethylether and the combined organic phases concentrated *in vacuo*. The product [1 g (100%) with contaminations of stereoisomers] is recrystallized twice from a mixture of *n*-hexane/C_6H_6. – Long colourless needles with a tendency to sublime (stereoisomer content < 5% by NMR); m.p. 184.5-186°C [closed tube; after recrystallization from 60-perc. EtOH: 172-184°C (diasteroisomers)]. – Comparable results were obtained using DIBAL. – IR (KBr): $\tilde{\nu}$ = 3200-3450 cm^{-1} (OH). – $[\alpha]_D^{20}$ = +101° ($CHCl_3$, c = 1, d = 1 dm). – ^{1}H NMR ($CDCl_3$)[12,14]: δ = 0.77 (H-9, H-9'), 0.90 (H-10, H-10'), 0.98 (H-5*endo*, H-5'*endo*), 1.05 (H-6*endo*, H-6'*endo*), 1.15 (H-8, H-8'), 1.45 (H-6*exo*, H-6'*exo*), 1.64 (H-4, H-4'), 1.69 (H-5*exo*, H-5'*exo*), 2.04 (H-3*endo*, H-3'*endo*), 2.46 (OH, OH'), 3.74 (H-2*endo*, H-2'*endo*); $^3J_{2endo,3endo}$ = 8.0 Hz, $^3J_{2endo,OH}$ = 2.62 Hz, $^4J_{2endo,3'endo}$ = -0.81 Hz, $^3J_{3endo,3'endo}$ = 13.2 Hz[12] [strong NOE between H-2 and H-3 (NOESY-spectra): *endo,endo*-position of H-2 and H-3; no coupling between H-3*endo* and H-4, H-4 doublet shows only coupling to H-5*exo* ($^3J_{4,5exo}$ = 4 Hz): *exo,exo*-bonding between bornane units]. – ^{13}C NMR ($CDCl_3$)[12,14]: δ = 11.8 (C-10, C-10'), 21.8 (C-8, C-8'), 22.3 (C-9, C-9'), 29.8 (C-5, C-5'), 34.0 (C-6, C-6'), 46.9 (C-7, C-7'), 34.0 (C-6, C-6'), 49.5 (C-1, C-1'), 49.8 (C-4, C-4'), 51.3 (C-3, C-3'), 83.0 (C-2, C-2'). – MS (70 eV), *m/z* (%): 306 (2) [M^+], 288 (19) [$M^+ - H_2O$], 272 (4) [$M^+ - H_2O - O$]. – $C_{20}H_{34}O_2$ (306.4): calcd. C 78.38, H 11.18; found C 77.99, H 11.24.

2-*endo*,3-*endo*,4-*endo*,5-*endo*-Tetrahydro-(1*R*,1'*R*)-diborn-2-eno[2,3-*b*;3',2'-*d*]furan (**18**). – A mixture of 310 mg (1 mmol) **16** and 300 mg Me_3OBF_4 is stirred 3 d at ambient temperature to yield a dark coloured solution. After concentration under reduced pressure the resulting solid (300 mg) is purified by CC [*n*-hexane/C_6H_6 (1:1)]. The product is obtained as second fraction and recrystallized twice from EtOH/H_2O (5:1). – Colourless spear-like crystals; yield: 180 mg (63%); m.p. 109-110°C (from 90°C sublimation). – $[\alpha]_D^{26}$ = +39° ($CHCl_3$, 40 mg/2 ml, d = 0.5 dm). ^{1}H NMR ($CDCl_3$)[11a,b,15]: δ = 0.78 (H-9, H-9'), 0.84 (H-6*endo*, H-6'*endo*), 0.91 (H-5*endo*, H-5'*endo*), 0.92 (H-10, H-10'), 0.96 (H-8, H-8'), 1.33 (H-6*exo*, H-6'*exo*), 1.66 (H-4, H-4'), 1.67 (H-5*exo*, H-5'*exo*), 2.06 (H-3*endo*, H-3'*endo*), 3.93 (H-2*endo*, H-2'*endo*); no coupling between H-3/H-3' and H-4/H-4': *endo*-position of H-3/H-3'). – ^{13}C NMR ($CDCl_3$)[11a,b,15]: δ = 11.5 (C-10, C-10'), 19.6 (C-8, C-8'), 23.1 (C-9, C-9'), 29.0 (C-5, C-5'), 33.2 (C-6, C-6'), 45.9 (C-7, C-7'), 49.0 (C-1, C-1'), 50.2 (C-4, C-4'), 56.7 (C-3, C-3'), 95.7 (C-2, C-2'). – MS (70 eV), *m/z* (%): 288 (100) [M^+], 273 (7) [$M^+ - CH_3$], 245 (32) [$M^+ - C_3H_7$], 177 (29) [dihydrobornenofuryl$^+$], 95 (41) [$C_7H_{11}^+$]. – $C_{20}H_{32}O$ (288.5): calcd. C 83.27, H 11.18; found C 82.72, H 11.12.

Δ^2-Tetrahydro-(1*R*,1'*R*)-diborn-2-eno[2,3-*c*;3',2'-*e*]pyridazine (19).– 298 mg (1 mmol) **11** are treated with 190 mg (5 mmol) $LiAlH_4$ in diethylether as described under **16**. – Colourless needles; yield: 249 mg (83%); m.p. 149-150°C. – IR (KBr): $\tilde{\nu}$ = 3290 cm^{-1} (s, NH), 1630 (s, C=N), 1580 (m, NH). – $[\alpha]_D^{20}$ = -46° ($CHCl_3$, c = 1, d = dm). – ^1H NMR ($CDCl_3$)[11a]: δ = 0.82, 0.84, 0.86, 0.90, 0.96 (5 CH_3), 1.02 (H-5'$_{endo}$), 1.11 (H-6'$_{endo}$), 1.21 (H-5$_{endo}$), 1.27 (CH_3), 1.47 (H-6'$_{exo}$), 1.50 (H-6$_{endo}$), 1.64 (H-4'), 1.65 (H-6$_{exo}$), 1.73 (H-3'$_{endo}$), 1.74 (H-5'$_{exo}$), 1.77 (H-4), 1.84 (H-3$_{endo}$), 1.88 (H-5$_{exo}$), 2.84 (H-2'$_{endo}$), 5.02 (NH); $^3J_{2'endo,3'endio}$ = 8.6 Hz, $^3J_{3'endo,3endo}$ = 9.0 Hz, $^3J_{4,5exo}$ = 3.9 Hz [no coupling between H-3 and H-4 as well as H-3' and H-4': H-3 and H-3' in *endo*-position; NOE between H-2'$_{endo}$ and H-3'$_{endo}$ as well as H-2'$_{endo}$ and H-6'$_{endo}$: H-2' and H-3' in *endo*-position]. – ^{13}C NMR ($CDCl_3$)[11a]: δ = 10.5, 11.5, 20.4, 20.8, 22.84, 22.81 (6 CH_3), 29.5 (C-5), 29.9 (C-5'), 31.3 (C-6), 35.4 (C-6'), 42.8 (C-3), 42.8 (C-3'), 47.9 (C-7'; exchangeable with C-7, C-1, C-1'), 48.1 (C-7, exchangeable with C-7', C-1, C-1'), 48.2 (C-1'; exchangeable with C-1, C-7, C-7'), 49.7 (C-4'), 50.1 (C4), 50.8 (C-1; exchangeable with C-1', C-7, C-7'), 63.6 (C-2'), 171.2 (C-2). – MS (70 eV), *m/z* (%): 300 (37) [M^+], 285 (4) [$M^+ - CH_3$], 272 (2) [$M^+ - N_2$], 231 (37) [$M^+ - N_2 - C_3H_7$], 189 (100) [$M^+ + H - N_2 - CH_3 - C_2H_2 - C_3H_7$]. – $C_{20}H_{32}N_2$ (300.4): calcd. C 79.95, H 10.74, N 9.31; found C 79.51, H 10.82, N 9.04.

6-*endo*-Methyl-Δ^2-tetrahydro (1*R*,1'*R*)-diborn-2-eno[2,3-*c*;3',2'-*e*]pyridazine (20).– A 1.6 molar solution of MeLi (7.5 ml) is added dropwise with stirring under an argon atmosphere at -30°C to a solution of 450 mg **11** in 25 ml abs. THF. After further stirring 30 min at -30°C, 2 h at 20°C and 2 h at 50°C, the mixture is hydrolyzed by careful addition of 50 ml H_2O at 0°C followed by twice extraction with 30 ml diethylether at a time. The mixture is then extracted twice with diethylether (2 x 30 ml) and the residue, after removal of the solvent, recrystallized from 70-perc. EtOH. – Colourless leaflets; yield: 355 mg (72%); m.p. 127-128°C. – IR (KBr): $\tilde{\nu}$ = 3280 cm^{-1} (m, NH), 1650 (s, C=N). – $[\alpha]_D^{20}$ = -170° ($CHCl_3$, c = 1, d = dm). – X-ray analysis in *Figure 2*[5b,c]. – ^1H NMR ($CDCl_3$)[11a]: δ = 0.83, 0.86, 0.86, 0.89, 0.99, 1.18 (6 CH_3), 1.01 (H-5'$_{endo}$), 1.19 (H-5$_{endo}$), 1.30 (H-6'$_{endo}$), 1.35 (CH_3-11'), 1.46 (H-3$_{endo}$), 1.53 (H-6$_{endo}$), 1.57 (H-6'$_{exo}$), 1.63 (H-4'), 1.65 (H-6$_{exo}$), 1.73 (H-4), 1.77 (H-5'$_{exo}$), 1.88 (H-5$_{exo}$), 1.94 (H-3'$_{endo}$), 4.46 (NH); $^3J_{4,5exo}$ = 3.0 Hz, $^3J_{4',5'exo}$ = 4.5 Hz [$^3J_{3,4}$ = 0 Hz, $^3J_{3',4'}$ = 0 Hz: H-3 and H-3' in *endo*-position; NOE between H-3'$_{endo}$ and CH_3-11': both in *endo*-position]. ^{13}C NMR ($CDCl_3$)[11a]: δ = 9.5, 10.5, 20.4, 20.8, 23.5, 26.5 (6 CH_3), 24.0 (CH_3-11'), 29.3 (C-5'), 29.7 (C-5), 31.0 (C6'), 31.5 (C-6), 43.8 (C-3'), 47.9 (C-4), 49.3 (C-7/C-7'), 49.8 (C-7/C-7'), 50.0 (C-4'), 50.9, 51.9 (C-1/C-1'), 56.5 (C-3), 65.1 (C-2'), 171.3 (C-2). – MS (70 eV), *m/z* (%): 314 (9) [M^+], 299 (13) [$M^+ - CH_3$], 271 (2) [$M^+ - N_2 - CH_3$], 245 (8) [$M^+ - N_2 - CH_3 - C_2H_2$], 202 (100) [$M^+ - N_2 - CH_3 - C_2H_2] - C_3H_7$]. – $C_{21}H_{34}N_2$ (314.5): calcd. C 80.25, 10.83, N 8.92; found C 79.89, H 11.04, N 8.88.

2-*endo*,3-*endo*,4-*endo*,5-*endo*-Tetrahydro-(1*R*,1'*R*)-diborn-2-eno[2,3-*b*;3',2'-*d*]thiophen-2-*endo*-thiol (21). – A stirred solution of 334 g (1 mmol) **3** in 10 ml benzene and 5 ml EtOH is treated under an argon atmosphere with 380 mg (10 mmol) $NaBH_4$. After 12 h the termination of the reaction is indicated by a colour change from orange red to pale yellow. The mixture is hydrolyzed by the addition of dilute HCl and then diluted with 30 ml benzene. The organic phase is separated, washed with water (2 x 20 ml) and concentrated. The residue is crystallized from 70-perc. EtOH. – Colourless needles; yield: 309 mg (92%); m.p. 110-111°C. – UV (MeCN): λ_{max} (lg ε): 220 nm (2.75), 240 (2.15, sh.). – $[\alpha]_D^{20}$ = -18° ($CHCl_3$, c = 1, d = 1 dm). – ^1H NMR ($CDCl_3$)[11a,c]: δ = 0.85, 0.88, 0.93, 1.15, 1.20, 1.51 (6 CH_3), 1.01 (H-5$_{endo}$), 1.01 (H-6$_{endo}$), 1.16 (H-5'$_{endo}$), 1.42 (H-6'$_{endo}$), 1.59 (H-6$_{exo}$), 1.74 (H-5'$_{exo}$), 1.78 (H-4'), 1.80 (H-5$_{exo}$), 1.86 (H-4), 1.92 (H-6'$_{exo}$), 2.46 (H-3$_{endo}$), 2.76 (H-3'$_{endo}$), 2.80 (SH), 3.40 (H-2$_{endo}$); $^3J_{4',5'exo}$ = 5.0 Hz, $^3J_{4,5exo}$ = 4.3 Hz, $^3J_{3'endo,3endo}$ = 5.2 Hz, $^3J_{2endo,3endo}$ = 9.8 Hz [coupling of H-3' only with H-3 but not with H-4', also strong NOE to H-5'$_{endo}$ (distance 2.2 Å, Alchemy): H-3' in *endo*-position; coupling of H-3 only with H-2 and H-3' but not with H-4, also strong NOE to H-5$_{endo}$ (distance 2.2 Å, Alchemy): H-3 in *endo*-position; coupling of H-2 only with H-3$_{endo}$, strong NOE to H-3$_{endo}$ (distance 2.3 Å, Alchemy) and to H-6$_{endo}$ (distance 2.2 Å, Alchemy): H-2 in *endo*-position]. – ^{13}C NMR ($CDCl_3$)[11a,c]: δ = 12.2, 13.5, 20.6, 22.3, 22.9, 24.7 (6 CH_3), 27.9 (C-5'), 29.6 (C-

5), 32.8 (C-6'), 37.3 (C-6), 47.6, 48.6, 48.9 (C-1, C-7, C-7'), 51.5 (C-4), 53.1 (C-4'), 56.1 (C-1'), 66.9 (C-3), 68.9 (C-2), 72.6 (C-3'), 81.9 (C-2'). – MS (70 eV), *m/z* (%): 336 (10) [M^+], 303 (100) [$M^+ - SH$], 287 (13) [$M^+ - H_2S - CH_3$], 259 (13) [$M^+ - H_2S - C_3H_7$]. – $C_{20}H_{32}S_2$ (336.6): calcd. C 71.43, H 9.52, S 19.05; found C 71.02, H 9.44, S 19.27. –

References and Notes

☆ *Dedicated to Professor Hans Suschitzky on the occasion of his 80th birthday*

1. a) Part I: Schroth, W.; Hintzsche, E.; Spitzner, R.; Ströhl, D.; Sieler, J. *Tetrahedron* **1995**, *51*, in press. – b) cf. also: Schroth, W.; Hintzsche, E.; Spitzner, R.; Irngartinger, H.; Siemund, V. *Tetrahedron Lett.* **1994**, *35*, 1973-1980.

2. a) Sen, D. C. *J. Indian Chem. Soc.* **1937**, *14*, 214-218. – b) Rây, P. C.; *Nature* **1936**, *138*, 548. – c) Campbell, M. M.; Evgenios, D. M. *J. Chem. Soc., Perkin Trans. 1*, **1973**, 2866-2869.

3. It should be emphasized that both sulfur atoms in **3** are very close to each other (distance of about 4.05 Å in the solid state) whilst both thiocamphor units are only slightly twisted towards each other (C4-C3-C3'-C4' torsion angle of 0.7°), as elucidated by X-ray crystallography in ref.[1b].

4. Jørgensen, K. A.; Ghattas, A.-B. G.; Lawesson, S. O. *Tetrahedron* **1982**, *38*, 1163-1168.

5. X-Ray structural analyses [Refinement by a full-matrix least squares method (SHELX 93)].
   a) Compound **9**: $C_{20}H_{28}OS$ (316.48), trigonal; space group: $P31_{Nr.144}$; a = 11.3700(10), b = 11.370(2), c = 12.1410(10) Å; α = β = 90°, γ = 120°; V = 135.9(3) $Å^3$; Z = 3; reflections collected: 1690, independent reflections: 1690 (R_{int} =0.0000); final R indices [I > 2σ(I)]: R1 = 0.0641, wR2 = 0.1864.
   b) Compound **20**: $C_{21}H_{34}N_2$ (314.50), triclinic; space group P1 (non-symmetric; presence of two symmetrically independent molecules within the same absolute configuration); a = 7.562 (2), b = 11.018(2), c = 13.101(3) Å, α = 109.10(2)°, β = 95.87(2)°, γ = 107.81(2)°; V = 956.8(4) $Å^3$; reflections collected: 3985, independent reflections: 3985 (R_{int} =0.0000); final R indices [I > 2σ(I)]: R1 = 0.0480, wR2 = 0.1251.
   c) Tables of the atomic coordinates, thermal parameters, bond lengths, and angles have been deposited at the Cambridge Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. The X-ray data for **9** and **20** are available on request from the Director of the CCDC by quoting the full literature citation of this paper.

6. Orito, K.; Yorita, K.; Miyazawa, M.; Suginome, H. *Synlett* **1994**, 937-938.

7. *For instance reaction of 3-bromocamphor with sodium:* a) Oddo, G. *Gazz. Chim. Ital.* **1893**, *23, II*, 314-335 (m.p. 128-130°C and 148-150°C); *ibid.* **1896**, *27,II*, 149-194 (m.p. 165-166°C). – b) Farbwerke Hoechst, DRP 94 498, **1896;** *Chem. Zentralbl.* **1898**, *69 I*, 295 (m.p. 165-166°C and 192-193°C). – c) Reznik, P. E. *Chem. Abstr.* **1959**, *53*, 9267d (m.p. 150-152°C; no steric information). – *Reaction of 3-bromocamphor with Grignard compounds (involving halogen-metal exchange in the primary step):* d): Malmgren, S. M. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2608-2642 (m.p. 151°C; wrongly characterized as „Campherpinakon"). – e) Agarwal, S. R. R.; Deshapande, S. S. *J. Indian Chem. Soc.* **1949**, *26*, 483-486 (m.p. 148°C, $[\alpha]_D$ = -128.7°C [EtOH]; obtained by reaction with EtMgI; wrongly characterized as „3-ethylcamphor"). – f) Briegleb, G.; Kuball, H. G.; Henschel, K. *Z. Phys. Chem.* **1965**, *46*, 229-246 (no steric informations; correction of structure assignment in ref.[7e]). – *Reaction of (R)-camphor with LDA and $CuCl_2$:* g) Itoh, Y.; Konoike, T., Harada, T.; Sagusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 1487-1493 (*exo-exo, exo-endo*, and *endo-endo* mixture). – *Reaction of 3-bromocamphor with $Co_2(CO)_8$ und PTC conditions:*

h) Alper, H.; Logbo, K. D.; des Abbayes, H. *Tetrahedron Lett.* **1977**, *33*, 2861-2864 (no further informations). – *Photolysis of 3-bromocamphor:* i) see ref.[6] (mixture of stereo isomers).

8. Cf.: a) Taipale, K. A. *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 243-245. – b) Mobbs, D. B.; Suschitzky, H. *J. Chem. Soc. [C]* **1971**, 175-178; (despite of a strongly acidic medium no rearrangement could be observed). – On the presumable preference of the *s-trans*-configuration: c) Kirste, K.; Poppek, R.; Rademacher, P. *Chem. Ber.* **1984**, *117*, 1061-1068.

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11. Assignments by: a) H,H-COSY, C,H-COSY and NOESY experiments, respectively; b) by APT; c) with the aid of DEPT.

12. Determination of the coupling constants by simulation with LAOCOON; cf.: Castellano, S.; Bothner-By, A. A. *J. Chem. Phys.* **1964**, *41*, 3863-3869.

13. Assignments based on: Bohlmann, F.; Zeisberg, R. *Org. Magn. Reson.* **1975**, *7*, 426-432.

14. Assignments based on values for isoborneol, a) for ^{1}H: Abraham, R.; Barlow, A. P.; Rowan, A. E. *Magn. Reson. Chem.* **1989**, *27*, 1074-1084; b) for ^{13}C: Duddeck, H.; Blagoev, B.; Berova, N.; Vassilev, V. *ibid.* **1983**, *21*, 122-124.

15. Assignments also by comparison with **16**.

(*Received in UK* 12 *September* 1995; *accepted* 5 *October* 1995)