75. Cob(I)alamin Differentiating Alkenes During Saturation[1])

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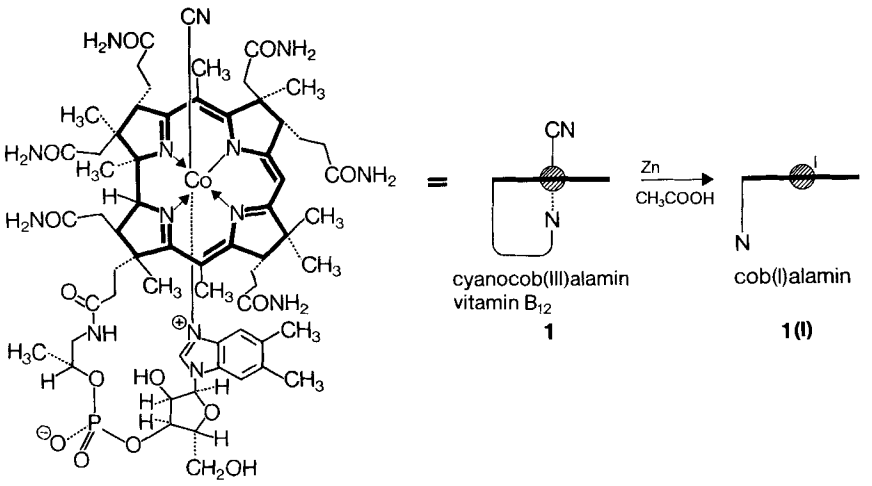
Summary

The olefins **2**, **7**, **11**, and **19** have been reduced using catalytic amounts of cob(I)alamin(**1(I)**). During a slow saturation, the catalyst is able to differentiate the two diastereotopic faces of the endocyclic double bonds in **11** ($t_{1/2}$ 40 d) and **19** ($t_{1/2}$ 80 d, *cf. Scheme 4*). The substrates **2** ($t_{1/2}$ 1 h, *cf. Scheme 2*) and **7** ($t_{1/2}$ 4 h, *cf. Scheme 3*) are reduced much faster. A rationalization of the data can be obtained formulating tertiary alkylcobalamins as intermediates. Of the oxime **6** *(cf. Scheme 2)* and the *p*-bromobenzoate **23** *(cf. Scheme 5)* the structures have been determined by X-ray analysis.

1. Introduction. – The saturation of olefins brought about by catalytic amounts of cob(I)alamin (**1(I)**; see *Scheme 1*) or by other Co-containing complexes is a well-known reaction. A recent review [2] on vitamin B_{12} and related Co-complexes as catalysts in

Scheme 1

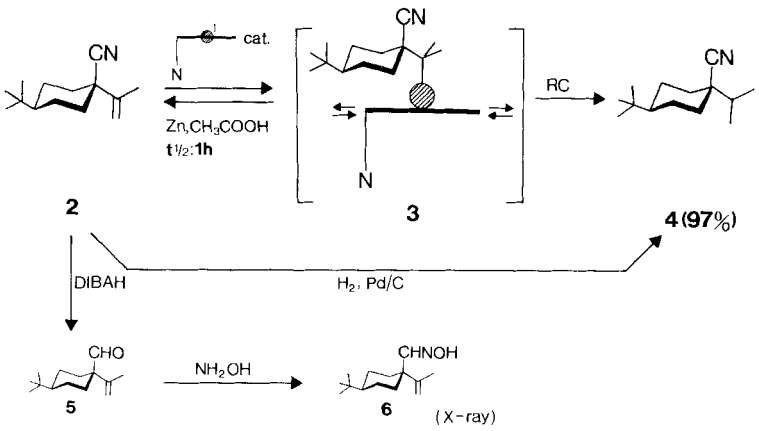


[1]) 11th Communication in the series 'Cob(I)alamin as Catalyst'; for the 10th communication see [1a].

organic synthesis also contains a compilation of the literature on cob(I)alamin-catalyzed saturation of olefins. The published data are not illustrating simple saturations[2]) of alkenes exclusively. Under the conditions used for such cob(I)alamin-catalyzed saturations, enantioselective reductions [3], isomerizations of isolated double bonds [1e], reductions of epoxides leading to the parent hydrocarbons [4], isomerization of allylic alcohols to aldehydes or ketones [1a] [1e], fragmentation of the carbon skeleton [5], and reductions of allylic alcohols to the corresponding hydrocarbons [1e] have been observed. The impact of these data on a mechanistic view will be discussed at the end of this paper.

2. Cob(I)alamin(1(I))-Catalyzed Saturations. – The cob(I)alamin-catalyzed reduction of the nitrile **2** (see *Scheme 2*) using glacial AcOH as solvent and as proton source and supplying the required electrons by an excess of granular Zn produced the saturated nitrile **4** in high yield[3]). Under the conditions applied, GC control showed a 50% consumption of the starting material after 1 h. In a blank experiment working without

Scheme 2



RC: reductive cleavage

cobalamin under parallel conditions, the starting material **2** was not transformed; no saturated nitrile **4** could be detected in the GC of the raw product. The saturation of the disubstituted double bond in **2** showed to be fast ($t_{1/2}$ 1 h) as compared to the saturation of the endocyclic olefin in **11** ($t_{1/2}$ 40 d, see *Scheme 4*). It is interesting to recognize that the nitrile function in **2** is not reduced, although the nitrile as well as the disubstituted olefin are placed in a sterically comparable arrangement. More accessible nitrile functions occupying sterically less crowded positions are reduced by cob(I)alamin(**1(I)**)[4]).

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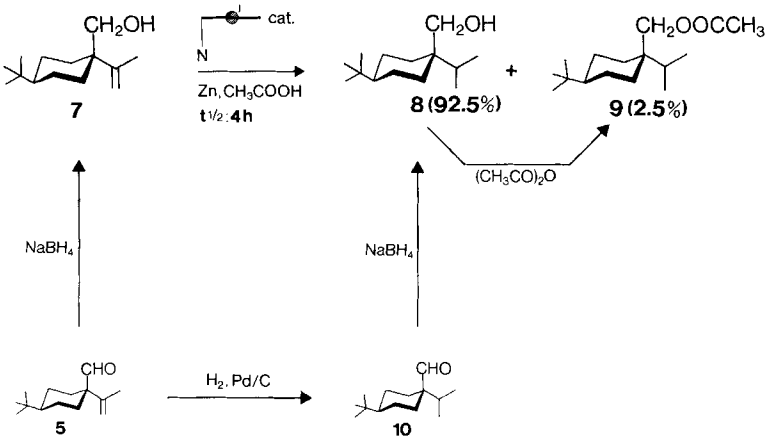
[2]) For saturation showing exclusively the expected saturated product see *e.g.* [1e]: *rac*-citronellol→*rac*-dihydrocitronellol.

[3]) Yield before chromatography 97% (GC); isolated material after chromatography: 92.5%.

[4]) Nitriles showing disubstituted or monosubstituted α-carbon atoms can be reduced by **1(I)** [1b] [1c].

As in earlier publications of this series, the initial formation of an intermediate tertiary alkylcobalamin **3**[5]) is formulated in the *Schemes* (see *e.g. Scheme 2*). At the end of this paper, the rationale supporting the formulation of intermediate alkylcobalamins is discussed. The Pd-catalyzed hydrogenation of **2** led to a saturated nitrile, which was identical with the product obtained from the cob(I)alamin-catalyzed reaction. We suppose, therefore, that the saturation catalyzed by **1(I)** proceeds without alteration of the carbon skeleton. To have a proof for the configuration of the starting material **2**, it was transformed to the oxime **6** from which crystals could be grown for X-ray analysis: Reduction of **2** with diisobutylaluminum hydride (DIBAH) and subsequent oxidation of the aldehyde **5** led to **6**.

Scheme 3

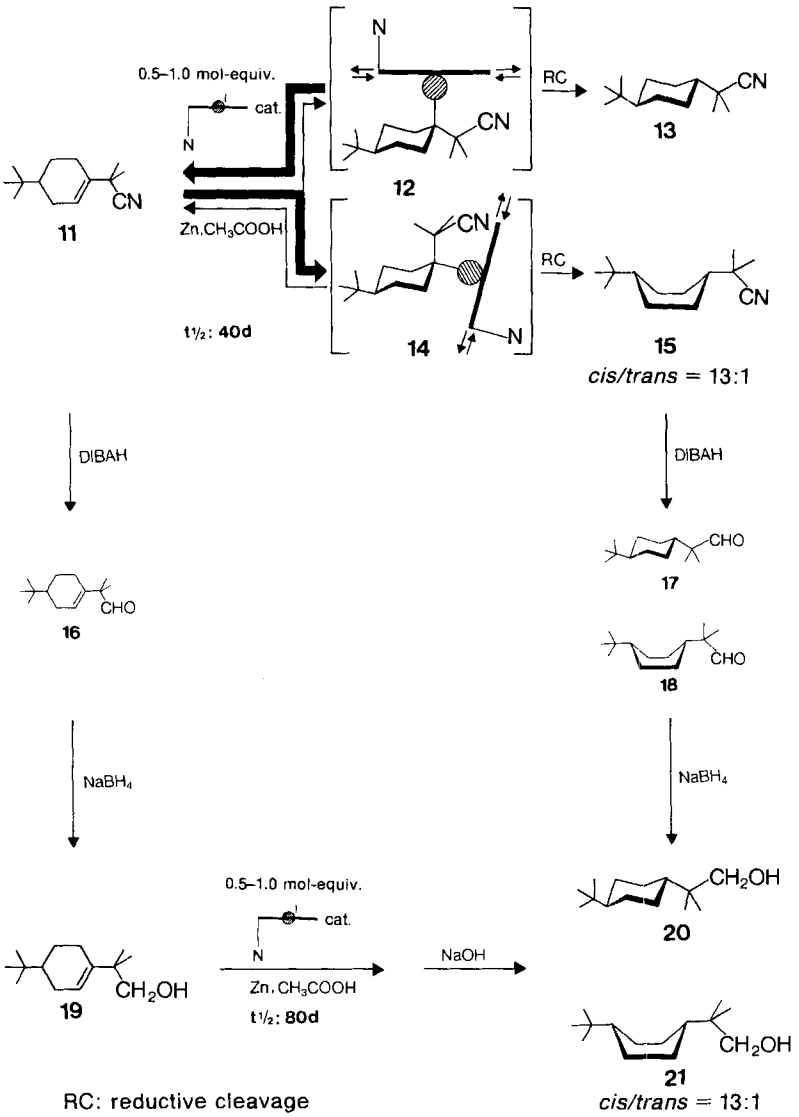


Cob(I)alamin-catalyzed saturation of the alcohol **7** (see *Scheme 3*), obtained after $NaBH_4$ reduction of **5**, produced the saturated alcohol **8** as well as the corresponding acetate **9**. After chromatography, **8** and **9** were isolated in 92.5 and 2.5% yield, respectively. GC control showed a fast saturation of the disubstituted olefin in **7** ($t_{1/2}$ 4 h) contrasting with the very slow saturation of the trisubstituted double bond in the alcohol **19** ($t_{1/2}$ 80 d, see *Scheme 4*). A blank experiment without cobalamin led to a raw product containing neither **8** nor **9**. The Pd-catalyzed hydrogenation of **5** produced the saturated aldehyde **10** from which an alcohol was accessible after $NaBH_4$ reduction. This alcohol was identical with **8**. We suppose therefore, a cob(I)alamin-catalyzed saturation of **7** proceeding without skeletal alterations. The acetylation of **8** led to the acetate **9** confirming the *trans*-relationship of the *tert*-butyl and the isopropyl group in **9**.

Starting with the olefin **11**, a very slow saturation was detected (see *Scheme 4*). Using higher amounts of cobalamin and a larger excess of granular Zn, the reduction was allowed to proceed for 50.3 d ($t_{1/2}$ 40 d) by repeating several times the same reaction after Zn consumption. The three nitriles **11**, **13**, and **15** could be isolated in 39.7,

[5]) The equilibrium of alkylcobalamins in solution is indicated by the lateral arrows. See *Footnote 2* in [4].

Scheme 4



3.5, and 45.6% yield, respectively. The saturated nitriles **15** *(cis)* and **13** *(trans)* were present in a 13:1 ratio. A blank experiment running for 27 days led to the starting material **11**; **13** and **15** could not be detected. If **12** and **14** are considered as intermediates, the observed *cis/trans*-ratio (**13**/**15** = 1:13) can be rationalized. Earlier experiments[6]) produced evidence for the presence of a fast equilibrium between alkylcobal-

[6]) *Cf. Chap. 5* and [1e].

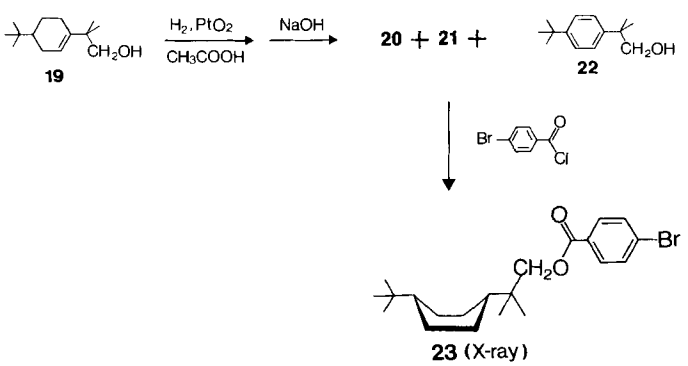
amins and the corresponding olefins under the conditions applied. This evidence transferred to the saturation of **11** implies the presence of an equilibration between **12** and **14**, **11** being the link connecting the two alkylcobalamins. Under thermodynamic control, **14** should prevail showing both the bulky *tert*-butyl substituent and the cobalamin system in equatorial positions. In **12** either the cobalamin or the *tert*-butyl group, *i.e.* in both cases the larger of the residues sitting on the two substituted ring C-atoms, has to adopt an axial arrangement. Assuming comparable kinetics during the reductive cleavage of the Co–C bond in **12** and **14** and taking the retention of configuration in this transformation into account [2] [5], the *cis*-substituted nitrile **15** should be produced in higher amounts. The arrangement of the two substituents in **15** is proven by its connection to the *p*-bromobenzoate **23** (see *below*).

The nitrile **11** was reduced to the aldehyde **16** using DIBAH. A subsequent $NaBH_4$ reduction led to **19**. During cob(I)alamin-catalyzed reduction, the alcohol **19** showed a rather resistant endocyclic olefin. This parallels the kinetics observed during the saturation of the trisubstituted double bond in the unsaturated nitrile **11**. Using a larger excess of metallic Zn and higher amounts of cobalamin, the reaction was allowed to proceed for 79 d ($t_{1/2} \approx 80$ d) by repeating several times the same reaction sequence after Zn consumption. After saponification of the acetates (*cf.* also *Scheme 3*), the three alcohols **19**–**21** could be isolated in 50.6, 2.6, and 33.9% yield, respectively. The saturated alcohols **21** *(cis)* and **20** *(trans)* were again present in a 13:1 ratio (GC). The *cis*/*trans* ratio of the saturated products can be explained in the same way as the ratio **15**/**13** (see *above*). A blank experiment running for one month without cobalamin led, after hydrolysis of the acetate, to the starting material **19**; **20** and **21** could not be detected.

To link the nitrile **13** with the alcohol **20** and **15** with **21**, the mixture obtained after repeated cob(I)alamin-mediated reduction of **11** was reduced to the aldehydes **17**/**18** using DIBAH. A subsequent $NaBH_4$ reduction led to two alcohols which showed to be identical with the alcohols **20** and **21** obtained after cob(I)alamin-mediated saturation of **19**. The *cis*-arrangement of the two substituents on the cyclohexane ring of **21** is proven by its transformation to the *p*-bromobenzoate **23** (see *below*).

The Pt-catalyzed hydrogenation of **19** in glacial AcOH (see *Scheme 5*) followed by saponification of the by-products (acetates) led to the formation of **20** and **21** as well as

Scheme 5



to minor amounts of the aromatic derivative **22**. As in the case of the cobalamin-catalyzed reductions of **2** and **7**, the corresponding saturations of **11** and **19**, therefore, also proceed without skeletal alterations.

The two saturated alcohols **20** and **21** (1:13) formed from **19** by cobalamin-dependent saturation could not be separated entirely by preparative GC or LC in order to grow crystals for X-ray analysis. Hence, the mixture **20/21** was transformed to the corresponding *p*-bromobenzoates *(cf. Scheme 5)*. Again preparative GC or LC did not allow to purify the major isomer. Therefore, crystals for X-ray analysis were grown from the *p*-bromobenzoate mixture. A single crystal was split into two pieces. One piece was used for X-ray crystallographic analysis, and the other was analyzed by capillary GC and shown to be devoid of the *p*-bromobenzoate from the minor isomer **20**. The X-ray analysis showed the major isomer **23** to be *cis*-substituted at the cyclohexane ring.

3. X-Ray Analyses.

Data were collected on a *Nicolet R3m* four-circle diffractometer fitted with a graphite monochromator. All calculations were carried out with the SHELXTL [6] package of the *R3m* system.

3.1. *X-Ray Data of the Oxime* **6**. *Crystal Data.* $C_{14}H_{25}NO$; mol. wt. 223.4, $F(000) = 496$; crystals from H_2O, m.p. 92–93°C. Space group and cell dimensions: monoclinic, $P2_1/n$; $a = 6.623(1)$, $b = 28.386(6)$, $c = 7.742(3)$ Å; $\beta = 98.07(3)°$; $D_x = 1.03$ Mg·m^{-3}, $Z = 4$. $\mu(CuK_\alpha) = 0.42$ mm^{-1}, absorption effects ignored.

Data Collection. Crystal size: 0.33 × 0.33 × 0.13 mm^3; temp. 293°K; $\lambda = 1.54189$ Å; Scan mode: ω; 4.0°/min minimum scan speed; strong reflections measured at up to 30°/min; scan width 2.0°; $0° \leq \theta < 57°$; peak/background ratio 2:1. Total data measured: 3040; total data observed: 1593; rejection criterion: $I < 2.5 \cdot \sigma(I)$; 167 parameters; $w = 1/(\sigma^2|F_o| + 0.001 \cdot |F_o|^2)$.

Structure Determination and Refinement. The structure was determined by direct methods using 32 starting phase permutations. Refinement proceeded smoothly to convergence at $R = 0.080$ with anisotropic refinement of all non-H-atoms. The position of the H-atom of the OH group was found from a difference map. The remaining H-atom coordinates were calculated using known geometries.

3.2. *X-Ray Data of the* p-*Bromobenzoate* **23**. *Crystal Data.* $C_{21}H_{31}BrO_2$; mol. wt. 395.4, $F(000) = 416$; crystals from MeOH, m.p. 83–84°C. Space group and cell dimensions: triclinic, $P\bar{1}$; $a = 6.199(3)$, $b = 10.457(5)$, $c = 16.083(11)$ Å; $\alpha = 96.14(5)$, $\beta = 90.31(5)$, $\gamma = 95.02(4)°$; $D_x = 1.27$ Mg·m^{-3}, $Z = 2$; $\mu(MoK_\alpha) = 1.98$ mm^{-1}.

Data Collection. Temp. 293°K; $\lambda = 0.71069$ Å. Scan mode: $\theta/2\text{-}\theta$; 6.0°/min minimum scan speed, strong reflections measured at up to 30°/min; scan width 1.8°; $0° \leq \theta < 25°$; peak/background ratio 2:1. Total data

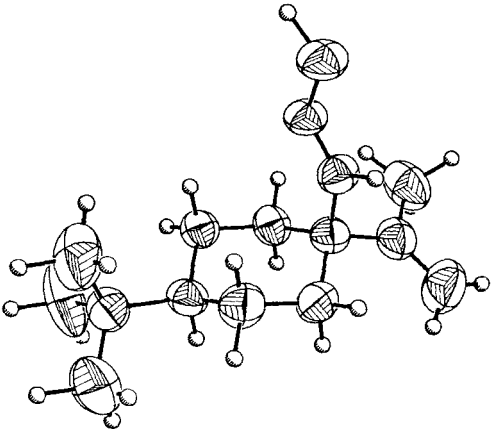


Fig. 1. *Perspective view of* **6** *with 50% probability ellipsoids*

measured: 3895; total data observed: 1338; rejection criterion: $I < 2.5 \cdot \sigma(I)$; number of parameters: 217; weights: $w = 1/(\sigma^2|F_o| + 0.001 \cdot |F_o|^2)$.

Structure Determination and Refinement. The structure was determined by direct methods. Refinement proceeded smoothly to convergence at $R = 0.068$ with anisotropic refinement of all non-H-atoms. The H-atom coordinates were calculated using known geometries.

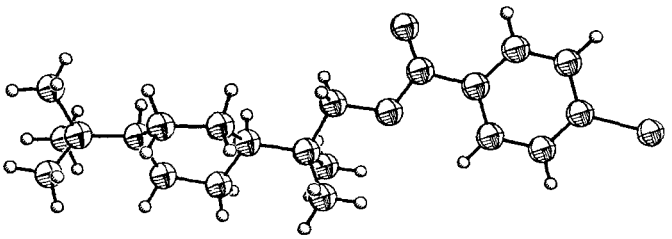
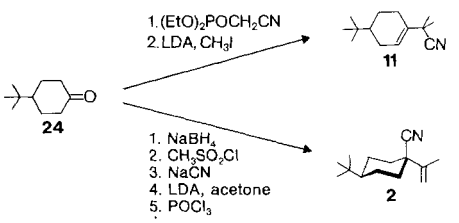


Fig. 2. *Perspective view of* **23** *with 50% probability ellipsoids*

4. Preparations of the Starting Materials. – For the preparation of **11**, 4-(*tert*-butyl)cyclohexanone (**24**) was transformed to (4-(*tert*-butyl)cyclohexylidene)acetonitrile using diethyl (cyanomethyl)phosphonate *(cf. Scheme 6)*. A subsequent treatment with lithium diisopropylamide (LDA) and methyl iodide led to the crystalline nitrile **11**. In order to prepare the nitrile **2**, 4-(*tert*-butyl)cyclohexanone (**24**) was reduced to a mixture of *cis*- and *trans*-(4-*tert*-butyl)cyclohexanol using $NaBH_4$. After a treatment with methanesulfonyl chloride and triethylamine, a mixture of *cis*- and *trans*-4-(*tert*-butyl)cyclohexyl methanesulfonates was obtained. A transformation with NaCN led to the two 4-(*tert*-butyl)cyclohexanecarbonitriles which were deprotonated with LDA. After quenching with acetone, 4β-(*tert*-butyl)-1α-(1-hydroxy-1-methylethyl)cyclohexanecarbonitrile was obtained. A dehydration using $POCl_3$ led to the nitrile **2**. This nitrile has been transformed to the oxime **6** (see *Scheme 2*) the configuration of which has been established by X-ray analysis (see *above*).

Scheme 6



5. Discussion. – Under the conditions applied[7]) as published in this and earlier papers [1a] reductions, isomerizations, and fragmentations, all catalyzed by **1(I)**, have

[7]) In most of the cases, 0.1 mol-equiv. of acetatocob(III)alamin (*cf.* **1**) prepared according to [1d], an excess of activated [1d] granular Zn, glacial or aqueous AcOH as solvent, and stirring at r.t. in the dark under Ar.

been observed. The system reduces allylic alcohols bearing an alkyl substituent in position 2 [1e] and epoxides [4] to the parent saturated hydrocarbons. It differenciates the two diastereotopic faces of olefins during saturation (*cf. above* and [1a] [5]) reducing *e.g.* α- or β-pinene to *cis*-pinane with high diastereoselectivity[8]). It leads to enantioselective saturation of olefins activated with electron withdrawing substituents [1d] [3] [7]. Under the same conditions, isomerizations of isolated [1e] and conjugated [1d] double bonds as well as transformations leading from allylic alcohols to saturated ketones [1a] or aldehydes [1e] have been reported. In addition, fragmentation of a strained carbon skeleton has been observed [5]. Evidence from these experiments taken together show that a 'close' contact between the olefin and cob(I)alamin (**1(I)**) is established during diastereoselective or enantioselective saturation. It has been shown that the isomerizations proceed much faster than the transformations leading to saturation [1e]. The characteristic pattern of position isomers resulting after migration of an isolated double bond can be rationalized considering an intermediate alkylcobalamin formed from an olefin, **1(I)**, and a proton following '*Markownikoff*'s' rule. The same intermediates allow the fragmentations to be explained. As there is a 'close' contact established between an olefin and **1(I)** during saturation, it is reasonable to formulate alkylcobalamins as intermediates portraying a concrete possibility of such a 'close' contact.

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Experimental Part

General Remarks. See [1b-e]. The procedure for the extraction is described in [1b] and the preparation of the catalyst in [1d]. AcOH = glacial acetic acid.

A. Starting Materials 2 and 11. – a) *4β-(*tert*-butyl)-1α-(1-methylvinyl)cyclohexanecarbonitrile* (**2**). To a solution of 200 g of 4-(*tert*-butyl)cyclohexanone (**24**) in 1.5 l of i-PrOH, 98.6 g of $NaBH_4$ were gradually added at 0°. Then, the mixture was stirred for 20 h at r.t. Aq. extraction (Et_2O) and crystallization (Et_2O/hexane) led to 156 g of *4β-(*tert*-butyl)cyclohexanol* (78%, mixture of stereoisomers). The crystals were dissolved in 1.3 l of CH_2Cl_2 and 400 ml of Et_3N. Then 150 ml of methanesulfonyl chloride in 300 ml of CH_2Cl_2 were added to the cold (0°) solution. The mixture was stirred at r.t. for 18 h. Aq. extraction (CH_2Cl_2) and crystallization (CH_2Cl_2/hexane, −30°) led to 122 g of *4-(*tert*-butyl)cyclohexyl methanesulfonate* (52%, mixture of stereoisomers). The crystalline material was dissolved in 1.5 l of hexamethylphosphoric triamide to which 510 g of NaCN were added. The suspension was stirred for 90 h at 50°. Aq. extraction (Et_2O) and chromatography (SiO_2, Et_2O/hexane) led to 42 g of *4-(*tert*-butyl)cyclohexanecarbonitrile* (51.7%, mixture of stereoisomers). Thereof 7.6 g in 75 ml of THF were slowly added to a cold solution (−78°) of 14.8 g of lithium diisopropylamide (LDA; 3 mol-equiv.) in 190 ml of THF, 70 ml hexane, and 20 ml of diisopropylamine. To this solution, 68.5 ml of acetone (20 mol-equiv.) were slowly added. The mixture was stirred at −78° for 2 h, the cooling bath removed, and stirring continued until r.t. was reached. The reaction was quenched with H_2O. Extraction (Et_2O), chromatographic purification (SiO_2, Et_2O/hexane), and crystallization (CH_2Cl_2/hexane) led to 5.9 g of *4β-(*tert*-butyl)-1α-(1-hydroxy-1-methylethyl)cyclohexanecarbonitrile* (57.5%). To 21 g of this material in 360 ml of $CHCl_3$, 211 ml of $POCl_3$ were slowly added. The solution was heated to reflux for 18 h. After aq. extraction (CH_2Cl_2) and chromatographic purification (SiO_2, CH_2Cl_2/hexane), 15.1 g (78.2%) of **2** were obtained, R_f 0.21 (CH_2Cl_2/hexane 1:2), t_R (GC, 100→280°) 8.3 min. IR (liq.): 3110 (C=CH_2); 2240 (C≡N); 1651 (C=C); 1460, 1400, 1373, 1245; 910 (C=CH_2). ^{1}H-NMR: 0.89 (*s*, 9H, $(CH_3)_3C$); 1.2–2.2 (*m*, 9H, 4CH_2, CH); 1.87 (br. *s*, 3H, CH_3); 4.94

[8]) *cis*-Pinane/*trans*-pinane 97:3 [5].

(br. *s*, 1H, *H*CH=C); 5.1 (*s*, 1H, HC*H*=C). ^{13}C-NMR (67.9 MHz): 19.82 (*q*, *C*H$_3$C=CH$_2$); 24.60 (2 *t*); 27.58 (3 *q*, (*C*H$_3$)$_3$C); 32.50 (*s*, (CH$_3$)$_3$*C*); 35.88 (2 *t*); 45.06 (*s*, C(1)); 47.76 (*d*, C(4)); 118.32 (*t*, *C*H$_2$=C); 122.08 (*s*, CN); 144.73 (*s*, CH$_2$=*C*). MS: 205 (1.5, M^+), 190 (9, $M^+ - CH_3$), 149 (40, $M^+ - (CH_3)_2CCH_2$), 134 (24), 121 (61), 107 (19), 57 (100, $(CH_3)_3C^+$), 41 (28).

b) *2-(4-*tert*-Butyl-1-cyclohexenyl)-2-methylproprionitrile* (**11**). To 68 g of diethyl (cyanomethyl)phosphonate in 200 ml of DMF at −20°, 28 g of NaOEt were added. After 30 min, 50 g of 4-(*tert*-butyl)cyclohexanone in 120 ml of DMF were added within 40 min. The mixture was warmed up to r.t. and stirring continued for additional 30 min. Aq. extraction (Et_2O), chromatographic purification (SiO_2, Et_2O/hexane) and crystallization (pentane) led to 39.7 g (69%, m.p. 55–56°) of *(4-(*tert*-butyl)cyclohexylidene)acetonitrile*. Thereof, 12.0 g in 60 ml of THF were added dropwise to a cold solution (−78°) of 65.4 g (9 mol-equiv.) of LDA in 300 ml of THF, 15 ml of diisopropylamine, and 300 ml of hexane. Then, 42 ml of MeI (10 mol-equiv.) were added dropwise, partly at −78° and partly at r.t. The mixture was stirred additionally at r.t. for 18 h. Using AcOH, the reaction was quenched, and aq. extraction (Et_2O), chromatographic purification (SiO_2, Et_2O/hexane), and crystallization (MeOH) led to 9.6 g (69%) of **11**, m.p. 37.5–38°, R_f 0.2 (CH_2Cl_2/hexane 1:2), t_R (GC, 100→300°) 10.4 min. IR (KBr): 2231 (C≡N); 1467, 1364, 1238. ^{1}H-NMR: 0.88 (*s*, 9H, $(CH_3)_3C$); 1.05–1.3 (*m*, 2H, H−C(4'), H_{ax}−C(5')); 1.42 (*s*, 3H, CH_3−C(2)); 1.43 (*s*, 3H, CH_3−C(2)); 1.65–2.30 (*m*, 5H, H_{eq}−C(5'), CH_2(3), CH_2(6)); 5.82 (br. *s*, 1H, H−C(2')). MS: 205 (8.5, M^+), 190 (5, $M^+ - CH_3$), 162 (4), 149 (8, $M^+ - CH_2{=}C(CH_3)_2$), 134 (10, $M^+ - CH_3{-}CH_2{=}C(CH_3)_2$), 122 (79, $M^+ - CH_2{=}C(CH_3)_2{-}HCN$), 107 (24), 81 (42), 69 (34), 57 (100, $(CH_3)_3C^+$).

B. Vitamin-B$_{12}$-catalyzed Reductions. – a) *Reduction* **2**→**4**. Following the procedure described earlier [1d], 1.32 g of cyanocob(III)alamin (**1**) were transformed to the catalyst. Prior to complete elimination of AcOH, the metallic Zn was removed by filtration. The red filtrate was evaporated to dryness at 50°, the residue dissolved in 60 ml of AcOH and 12.7 g (20 mol-equiv.) of activated [1d] metallic Zn were added. The suspension was stirred at r.t. under Ar until[9]) a dark green color revealed the presence of cob(I)alamin (**1(I)**). To the suspension of the soluble catalyst and granular Zn 2.0 g of **2** in 20 ml of AcOH were added[10]). The mixture was stirred in the dark at r.t. for 18 h under Ar. Following the usual extraction, the crude product (quant.; GC: 97% pure **4**) was purified by chromatography (SiO_2, CH_2Cl_2/hexane 1:2): 1.87 g (92.5%) of *4β-(*tert*-butyl)-1α-isopropyl-cyclohexanecarbonitrile* (**4**), m.p. 89–91° (MeOH), R_f 0.40 (CH_2Cl_2/hexane 1:1), t_R (GC, 100→280°) 5.8 min. IR (KBr): 2225 (C≡N); 1471, 1446, 1389, 1367. ^{1}H-NMR: 0.88 (*s*, 9H, $(CH_3)_3C$); 1.06 (*d*, J = 6.5, 6H, $(CH_3)_2CH$); 1.0–2.25 (*m*, 10H, 4CH$_2$, 2CH). MS: 207 (4, M^+), 192 (27, $M^+ - CH_3$), 179 (10), 165 (6), 150 (56, $M^+ - (CH_3)_3C$), 136 (57, $M^+ - CH_3{-}CH_2{=}C(CH_3)_2$), 123 (67), 108 (80), 81 (19), 57 (100).

A corresponding blank experiment without cobalamin led to the starting material **2**; no **4** could be detected.

b) *Reduction* **7**→**8** *and* **9**. From 1.03 g of cyanocob(III)alamin (**1**) the catalyst was prepared according to *B.a)*. To the suspension of the soluble catalyst, dissolved in 48 ml of AcOH, and 9.9 g of activated granular Zn, 1.6 g of **7** in 16 ml of AcOH were added. The mixture was stirred in the dark at r.t. for 18 h under Ar. Following the usual extraction, the crude mixture (1.57 g, 97%; GC: 95.5% **8** and 2.6% **9**) was separated by chromatography (SiO_2, CH_2Cl_2/hexane 4:1): 1.49 (92.5%) of **8** and 48.5 mg (2.5%) of **9**. *4β-(*tert*-Butyl)-1α-isopropyl-cyclohexanemethanol* (**8**): m.p. 95–96° (MeOH), R_f 0.23 (CH_2Cl_2/hexane 4:1), t_R (GC, 100→300°) 11.2 min. IR (KBr): 3302 (OH); 1468, 1363, 1088, 1045, 1008. ^{1}H-NMR: 0.83 (*s*, 9H, $(CH_3)_3C$); 0.89 (*d*, J = 7, 6H, $(CH_3)_2CH$); 0.85–1.80 (*m*, 10H, 4CH$_2$, 2CH); 1.21 (*s*, 1H, OH); 3.64 (*s*, 2H, CH$_2$O). MS (CI): 230 (100, $M + NH_4^+$), 211 (7), 193 (8), 180 (22), 168 (15), 151 (35), 137 (15), 123 (32), 122 (8), 109 (24), 95 (59), 81 (43), 79 (3), 67 (7), 57 (7), 35 (8).

*4β-(*tert*-Butyl)-1α-isopropyl-cyclohexanemethyl Acetate* (**9**): R_f 0.27 (CH_2Cl_2/hexane 1:1), t_R (GC, 100→300°) 13.1 min. IR (liq.): 1742 (C=O); 1469, 1449, 1365; 1240 (ester); 1036. ^{1}H-NMR: 0.83 (*s*, 9H, $(CH_3)_3C$); 0.86 (*d*, J = 7, 6H, $(CH_3)_2CH$); 0.85–1.80 (*m*, 10H, 4CH$_2$, 2CH); 2.04 (*s*, 3H, CH_3COO); 4.06 (*s*, 2H, CH_2O). MS: 211 (5, $M^+ - CH(CH_3)_2$), 194 (2.5, $M^+ - CH_3COOH$), 181 (2.5, $M^+ - CH_2OOCCH_3$), 168 (4.5), 151 (16, $M^+ - CH(CH_3)_2{-}CH_3COOH$), 138 (7.5), 125 (14), 109 (10), 95 (45), 81 (31), 69 (22), 57 (100, $(CH_3)_3C^+$), 43 (32).

A corresponding blank experiment without cobalamin led to the starting material **7**; no **8** and **9** could be detected.

c) *Reduction* **11**→**13** *and* **15**. From 6.6 g (1 mol-equiv.) of cyanocob(III)alamin (**1**), the cobalamin derivative required for reduction was prepared according to *B.a)*. To the suspension of cobalamin dissolved in 30 ml of

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[9]) For the development of the green color, a period of 5–10 min was usually required.

[10]) The color turned back to red owing to the access of air during the opening of the flask.

AcOH and 19.1 g (60 mol-equiv.) of activated granular Zn were added 1.0 g of **11** in 40 ml of AcOH. The mixture was stirred in the dark at r.t. for 4.3 d under Ar. Following the usual extraction, 980 mg (98%) of crude product were obtained. GC: only 5.5% of reduced nitrile. Using this crude product, cobalamin-dependent reductions were repeated several times using following conditions: 1) 0.5 mol-equiv. of **1**, 60 mol-equiv. of Zn, $AcOH/H_2O$ 20:1, 5 d at r.t., 99% of crude product; 2) 0.5 mol-equiv. of **1**, 60 mol-equiv. of Zn, AcOH, 7 d at r.t., 96% of crude product; 3) 0.5 mol-equiv. of **1**, 60 mol-equiv. of Zn, $AcOH/H_2O$ 10:1, 7 d at r.t., 92.5% of crude product; 4) 1.0 mol-equiv. of **1**, 70 mol-equiv. of Zn, AcOH, 7 d at r.t., 99% of crude product; 5) 1.0 mol-equiv. of **1**, 70 mol-equiv. of Zn, $AcOH/H_2O$ 10:1, 10 d at r.t., 95.5% of crude product; 6) 500 mg from the raw product obtained after 5), 1.0 mol-equiv. of **1**, 60 mol-equiv. of Zn, AcOH, 10 d at r.t., 96% of crude product (GC: 42.9% **11**, 3.8% **13**, 49.3% **15**). This raw product was purified by chromatography (SiO_2, Et_2O/hexane): 198.5 mg (39.7%) of **11**, 17.7 mg (3.5%) of **13**, 230 mg (45.6%) of **15**. *2-(*trans*-4-(*tert*-Butyl)cyclohexyl)-2-methylpropiononitrile* (**13**): R_f 0.2 (CH_2Cl_2/hexane 1:2), t_R (GC, 100→300°) 10.5 min. ^{1}H-NMR: 0.86 (*s*, 9H, $(CH_3)_3C$); 1.05–2.30 (*m*, 10H, $4CH_2$, 2CH); 1.32 (*s*, 6H, $(CH_3)_2C$).

*2-(*cis*-4-(*tert*-Butyl)cyclohexal)-2-methylpropiononitrile* (**15**): R_f 0.2 (CH_2Cl_2/hexane 1:2), t_R (GC, 100→300°) 10.15 min. ^{1}H-NMR: 0.86 (*s*, 9H, $(CH_3)_3C$); 1.05–2.3 (*m*, 10H, $4CH_2$, 2CH); 1.34 (*s*, 6H, $(CH_3)_2C$).

A blank experiment running for 27 d without cobalamin led to the starting material **11**; no **13**, **15**, and **4** could be detected.

d) *Reduction* **19→20** *and* **21**. From 2.59 g (0.5 mol-equiv.) of cyanocob(III)alamin (**1**), the cobalamin derivative required for reduction was prepared according to *B.a)*. To the suspension of cobalamin, dissolved in 30 ml of AcOH, and 14.9 g (60 mol-equiv.) of activated granular Zn were added 800 mg of **19** in 27 ml of AcOH. The mixture war stirred in the dark at r.t. for 6 d under Ar. Following the usual extraction and a subsequent hydrolysis using NaOH/MeOH to hydrolyze the acetates formed as by-products, 750 mg (94%) of a crude product were obtained. GC: only 5% of a saturated alcohol. Using this crude product, cobalamin-dependent reductions followed by NaOH/MeOH hydrolyses were repeated several times using the following conditions: 1) 1 mol-equiv. of **1**, 60 mol-equiv. of Zn, AcOH, 6 d at r.t., 91% of crude product; 2) 1 mol-equiv. of **1**, 60 mol-equiv. of Zn, AcOH, 21 d at r.t., 99% of crude product; 3) 1 mol-equiv. of **1**, 70 mol-equiv. of Zn, $AcOH/H_2O$ 10:1, 7 d at r.t., 93.4% of crude product; 4) 1 mol-equiv. of **1**, 70 mol-equiv. of Zn, $AcOH/H_2O$ 10:1, 12 d at r.t., 94% of crude product; 5) 1 mol-equiv. of **1**, 70 mol-equiv. of Zn, $AcOH/H_2O$ 10:1, 12 d at r.t., 96.5% of crude product; 6) 450 mg from the raw product obtained after 5), 1 mol-equiv. of **1**, 70 mol-equiv. of Zn, $AcOH/H_2O$ 10:1, 15 d at r.t., 99.4% of crude product (GC: 57.75% **19**, 2.95% **20**, 38.7% **21**). This raw product was purified by chromatography (SiO_2, CH_2Cl_2/hexane): 228 mg of **19** (50.6%), 11.8 mg of **20** (2.6%), and 153.5 mg of **21** (33.9%). Data of **19**: see *C.h*). *2-(*trans*-4(*tert*-Butyl)cyclohexyl)2-methylpropanol* (**20**): R_f 0.28 (Et_2O/hexane 2:3), t_R (GC, 50180°) 22.0 min. ^{1}H-NMR: 0.82 (*s*, 15H, $(CH_3)_3C$, $(CH_3)_2CCH_2OH$); 1.0–1.6 (*m*, 7H, H–C(1), H–C(4), H_{ax}–C(2), H_{ax}–C(3), H_{ax}–C(5), H_{ax}–C(6), OH); 1.6–2.2 (*m*, 4H, H_{eq}–C(2), H_{eq}–C(3), H_{eq}–C(5), H_{eq}–C(6)); 3.9 (*s*, 2H, CH_2O).

*2-(*cis*-4-(*tert*-Butyl)cyclohexyl)-2-methylpropanol* (**21**): R_f 0.28 (Et_2O/hexane 2:3), t_R (GC, 501→80°) 22.2 min. ^{1}H-NMR: 0.82 (*s*, 15H, $(CH_3)_3C$, $(CH_3)_2CCH_2OH$); 1.0–1.6 (*m*, 7H, H–C(1), H–C(4), H_{ax}–C(2), H_{ax}–C(3), H_{ax}–C(5), H_{ax}–C(6), OH); 1.6–2.2 (*m*, 4H, H_{eq}–C(2), H_{eq}–C(3), H_{eq}–C(5), H_{eq}–C(6)); 3.8 (*s*, 2H, CH_2O).

A blank experiment running for 1 month without cobalamin led, after hydrolysis of the acetate, to the starting material **19**; no **20**, **21**, and **8** could be detected.

C. **Additional Transformations.** – a) *DIBAH Reduction* **2→5**. To a solution of 14.9 g of **2** in 140 ml of dry Et_2O at −78°, 80 ml of 1M diisobutylaluminum hydride (DIBAH) in hexane (1.1 mol-equiv.) were added within 1/2 h. The mixture was stirred for 2 additional h at −78°. The cloudy suspension was carefully poured into 300 ml of stirred 5% aq. H_2SO_4 at 0°. After extraction (Et_2O), the raw product was purified by chromatography (SiO_2, Et_2O/hexane): 12.3 g (81.5%) of *4β-(*tert*-butyl)-1α-(1-methylvinyl)cyclohexanecarbaldehyde* (**5**). After crystallization, m.p. 35–36° (MeOH), R_f 0.36 (Et_2O/hexane 1:20), t_R (GC, 50→300°) 17.94 min. IR (KBr): 2694 (CHO); 1719 (C=O); 1628 (C=C); 1466, 1444, 1364; 913 (C=CH_2). ^{1}H-NMR: 0.82 (*s*, 9H, $(CH_3)_3C$); 0.88–1.0 (*m*, 1H, H_a–C(4)); 1.0 (*ddd*, J = 15, 14, 11, 2H, H_β–C(3), H_β–C(5)); 1.39 (*dd*, J = 13, 11, 2H, H_a–C(2), H_a–C(6)); 1.65 (*s*, 3H, CH_3); 1.72 (br. *d*, J = 14, 2H, H_a–C(3), H_a–C(5)); 2.34 (br. *d*, J = 13, 2H, H_β–C(2), H_β–C(6)); 4.9 (*s*, 1H, *H*CH=C); 5.03 (*s*, 1H, HC*H*=C); 9.19 (*s*, 1H, CHO). ^{13}C-NMR (100.62 MHz): 19.46 (*q*, CH_2=C–*C*H_3); 24.20 (2 *t*); 27.45 (3 *q*, $(CH_3)_3C$); 30.95 (2 *t*); 32.29 (*s*, $(CH_3)_3C$); 47.49 (*d*, C(4)); 55.74 (*s*, C(1)); 113.94 (*t*, CH_2=C); 144.29 (s, CH_2=C); 202.24 (*d*, CHO). MS: 208 (2, M^+), 193 (1.5, $M^+ - CH_3$), 179 (8, $M^+ - CHO$), 123 (38, $M^+ - CHO-CH_2=C(CH_3)_2$), 109 (61), 107 (5), 95 (20), 91 (5), 81 (27), 77 (5), 67 (20), 57 (100, $(CH_3)_3C^+$), 55 (20), 53 (7), 41 (39), 39 (9), 29 (19), 27 (7).

b) *Oxime Formation* **5→6**. To a solution of 316 mg of crystalline **5** in 5 ml of EtOH and 0.3 ml of pyridine, 316 mg of NH_2OH-HCl were added. The solution was heated under reflux for 70 h. After extraction (Et_2O), the product was purified by chromatography (SiO_2, Et_2O/hexane) and crystallized using pentane: 252 mg (74.5%) of *4β(* tert*-butyl)-1α-(1-methylvinyl)cyclohexanecarbaldehyde oxime* (**6**), m.p. 92–93°, R_f 0.14 (CH_2Cl_2/hexane 1:1), t_R (GC, 100→300°) 12.8 min. IR (KBr): 3262, 3161 (OH); 1632 (C=N); 1443, 1366; 905 (C=CH_2). ^{1}H-NMR: 0.83 (*s*, 9H, $(CH_3)_3C$); 0.97 (*tt*, *J* = 12, 3.5, 1H, H_a–C(4)); 1.23 (*dddd*, *J* = 13, 13, 12, 3.5, 2H, H_β–C(3), H_β–C(5)); 1.41 (*ddd*, *J* = 13, 13, 3, 2H, H_a–C(2), H_a–C(6)); 1.67 (br. *d*, *J* = 13, 2H, H_a–C(3), H_a–C(5)); 1.72 (*s*, 3H, CH_3); 2.11 (br. *d*, *J* = 13, 2H, H_β–C(2), H_β–C(6)); 4.83 (*s*, 1H, *H*CH=C); 4.85 (*s*, 1H, HC*H*=C); 7.10 (*s*, 1H, OH); 7.50 (*s*, 1H, CH=N). MS: 223 (15, M^+), 208 (22, $M^+ - CH_3$), 206 (14, $M^+ - OH$), 166 (15, $M^+ - (CH_3)_3C$), 124 (100), 111 (32), 57 (59, $(CH_3)_3C^+$), 41 (32).

c) *$NaBH_4$ Reduction* **5→7**. To a solution of 1.8 g of crystalline **5** in 25 ml of i-PrOH, 490 mg of $NaBH_4$ were added, and the mixture was stirred at r.t. for 18 h. Aq. extraction (Et_2O) led, after crystallization from petroleum ether (80–110°), to 1.51 g (83%) of *4β-(* tert*-butyl)-1α-(1-methylvinyl)cyclohexanemethanol* (**7**). M.p. 91–92° (MeOH), R_f 0.23 (CH_2Cl_2/hexane 1:1), t_R (GC, 100→280°) 6.7 min. IR (KBr): 3382, 3251 (OH); 1634 (C=C); 1364, 1052; 883 (C=CH_2). ^{1}H-NMR: 0.87 (*s*, 9H, $(CH_3)_3C$); 0.8–2.1 (*m*, 10H, $4CH_2$, CH, OH); 1.73 (br. *s*, 3H, CH_3); 3.55 (*s*, 2H, CH_2O); 4.83 (*s*, 1H, *H*CH=C); 4.95 (br. *s*, 1H, HC*H*=C). ^{13}C-NMR (67.9 MHz): 19.24 (*q*, CH_2=C–*C*H_3); 23.18 (2 *t*); 27.65 (3 *q*, *C*$(CH_3)_3C$); 32.11 (2 *t*); 32.52 (*s*, $(CH_3)_3$*C*); 43.40 (*s*, C(1)); 48.34 (*d*, C(4)); 62.78 (*t*, CH_2O); 111.76 (*t*, *C*H_2=C); 151.27 (*s*, CH_2=*C*). MS: 210 (1, M^+), 192 (3.7, $M^+ - H_2O$), 179 (37, $M^+ - CH_2OH$), 123 (67, $M^+ - CH_2OH$–$(CH_3)_2CCH_2$), 109 (58), 95 (35), 81 (38), 69 (28), 57 (100, $(CH_3)_3C^+$), 41 (34).

d) *Pd-catalyzed Hydrogenation* **5→10**. To 1.0 g of crystalline **5** in 10 ml of MeOH, was added 1.0 g of 10% Pd/C. The suspension was stirred at r.t. under H_2 for 1 week. After filtration and chromatographic purification (SiO_2, CH_2Cl_2/hexane), the product was crystallized from cold MeOH: 485 mg (48%) of *4β-(* tert*-butyl)-1α-isopropyl-cyclohexanecarbaldehyde* (**10**), m.p. 29–31°, R_f 0.38 (CH_2Cl_2/hexane 1:1), t_R (GC, 100→300°) 9.1 min. IR (liq.): 1693 (C=O); 1469, 1364. ^{1}H-NMR: 0.82 (*s*, 9H, $(CH_3)_3C$); 0.88 (*d*, *J* = 7, 6H, $(CH_3)_2CH$); 0.85–2.3 (*m*, 10H, $4CH_2$, 2CH); 9.47 (*s*, 1H, CHO). MS: 210 (3, M^+), 181 (7, $M^+ - CHO$), 155 (24), 125 (35, $M^+ - CHO - CH_2$=$C(CH_3)_2$), 111 (19), 95 (20), 81 (31), 69 (52), 57 (100, $(CH_3)_3C^+$), 41 (40).

e) *$NaBH_4$ Reduction* **10→8**. As in *C.c)*, 115 mg of crystalline **10** in 5 ml of i-PrOH were reduced with 42 mg of $NaBH_4$ and worked up. Chromatographic purification (SiO_2, CH_2Cl_2/hexane) and crystallization (MeOH) gave 94 mg of **8** (81%). Data: *cf. B.b)*.

f) *Acetylation* **8→9**. The solution of 300 mg of crystalline **8** in 5 ml of pyridine and 0.7 ml of Ac_2O was stirred at r.t. for 18 h. After aq. extraction (Et_2O) and chromatographic purification (SiO_2, Et_2O/pentane), 295 mg of **9** (82%) were obtained. Data: *cf. B.b)*.

g) *DIBAH Reduction* **11→16**. As in *C.a)*, 7.5 g of **11** in 70 ml of Et_2O were reduced with 40 ml of 1M DIBAH (stirring for 2.5 h). To quench the reduction, 10 ml of AcOH were added at −78°. After aq. extraction (Et_2O) and chromatographic purification (SiO_2, Et_2O/hexane), crystallization (MeOH) led to 5.93 g (78%) of *2-(4-(* tert*-butyl)-1-cyclohexenyl)-2-methylpropionaldehyde* (**16**), m.p. 61–62°, R_f 0.25 (Et_2O/hexane 1:20), t_R (GC, 50→300°) 18.7 min. IR (KBr): 2796, 2694 (CHO); 1733, 1721 (C=O); 1657 (C=C); 1466, 1392, 1363. ^{1}H-NMR: 0.86 (*s*, 9H, $(CH_3)_3C$); 1.14 (*s*, 3H, CH_3); 1.16 (*s*, 3H, CH_3); 1.0–1.3 (*m*, 2H, H–C(4), H_{ax}–C(5)); 1.75–2.0 (*m*, 4H, CH_2(3), CH_2(6)); 2.0–2.2 (*m*, 1H, H_{eq}–C(5)); 5.6 (br. *s*, 1H, H–C(2)); 9.27 (*s*, 1H, CHO). ^{13}C-NMR: 20.15, 20.49 (2 *q*, $(CH_3)_2$CCHO); 24.30 (*t*); 26.66 (*t*); 27.12 (3 *q*, *C*H_3)$_3$C); 27.30 (*t*); 32.11 (*s*, $(CH_3)_3$*C*); 43.74 (*d*, C(4)); 51.28 (*s*, $(CH_3)_2$*C*CHO); 124.84 (*d*, C(2)); 136.72 (*s*, C(1)); 203.125 (*d*, CHO). MS (CI): 226 (33, $M + NH_4^+$), 209 (25, $M + H^+$), 179 (32), 137 (3), 123 (8), 109 (7), 95 (3), 35 (100).

h) *$NaBH_4$ Reduction* **16→19**. As in *C.c)*, 2.26 g of **16** in 40 ml of EtOH were reduced with 607 mg of $NaBH_4$. After aq. workup (Et_2O) and chromatographic purification (SiO_2, Et_2O/hexane), crystallization (pentane) led to 1.93 g (84.5%) of *2-(4-(* tert*-butyl)-1-cyclohexenyl)-2-methylpropanol* (**19**), m.p. 82–84°, R_f 0.28 (Et_2O/hexane 2:3), t_R (GC, 100→180°) 21.3 min. IR (KBr): 3415, 3253 (OH); 1633 (C=C); 1469, 1454, 1363, 1048, 1032. ^{1}H-NMR: 0.86 (*s*, 9H, $(CH_3)_3C$); 1.01 (*s*, 3H, CH_3); 1.08 (*s*, 3H, CH_3); 1.0–1.5 (*m*, 3H, H–C(4), H_{ax}–C(5), OH); 1.5–2.2 (*m*, 5H, CH_2(3), CH_2(6), H_{eq}–C(5)); 3.36 (*ABX*, J_{AB} = 12, $J_{AX} = J_{BX}$ = 6.5, 2H, CH_2O); 5.5–5.7 (*m*, 1H, H–C(2). MS: 210 (8, M^+), 179 (70, $M^+ - CH_2OH$), 123 (98, $M^+ - CH_2OH$–$(CH_3)_2CCH_2$), 109 (64), 95 (36), 57 (100, $(CH_3)_3C^+$).

i) *DIBAH Reduction* **13/15/11→16–18**. To 302 mg of **13/15/11** (obtained after repeated vitamin-B_{12}-catalyzed reduction of **11**) in 5 ml of dry Et_2O at −78°, 2.0 ml of 1M DIBAH in hexane were added. Stirring was continued for 2 h at −78°. Aq. extraction (Et_2O) and chromatographic purification (SiO_2, Et_2O/hexane) led to 282 mg of **17/18/16** (93% of the material recovered). Data of **16**: *cf. C.g)*. *2-(*trans*-4-(* tert*-Butyl)cyclohexyl)-2-*

methylpropionaldehyde (**17**): R_f 0.23 (Et_2O/hexane 1:20), t_R (GC, 50→150°) 17.9 min. ^{1}H-NMR: 0.82 (*s*, 9H, $(CH_3)_3C$); 0.99 (*s*, 6H, $2CH_3$); 1.0–2.2 (*m*, 10H, $4CH_2$, 2CH); 9.46 (*s*, 1H, CHO).

*2-(*cis*-4-(*tert*-Butyl)cyclohexyl)-2-methylpropionaldehyde* (**18**): R_f 0.23 (Et_2O/hexane 1:20), t_R (GC, 50→150°) 18 min. ^{1}H-NMR: 0.82 (*s*, 9H, $(CH_3)_3C$); 1.05 (*s*, 6H, $2CH_3$); 1.0–2.2 (*m*, 10H, $4CH_2$, 2CH); 9.49 (*s*, 1H, CHO).

k) *$NaBH_4$ Reduction* **17/18/16→19–21**. As in *C.c)*, 252 mg of **17/18/16** (see *C.i)*) in 15 ml of i-PrOH were reduced with 100 mg of $NaBH_4$ and worked up. Chromatographic purification (SiO_2, Et_2O/hexane) gave 231 mg of **20/21/19** (91% of the material recovered). Data of **19–21**: see *B.d)*, *C.h)*.

l) *PtO_2 Hydrogenation* **19→20–22.** To 777 mg of **19** in 50 ml of AcOH were added 270 mg of PtO_2. The suspension was hydrogenated during 4 d at r.t. After aq. workup (Et_2O), the crude product was treated with an excess of NaOH in MeOH to saponify the acetates partially formed. After aq. workup (Et_2O), the product was purified by chromatography (SiO_2, Et_2O/hexane) allowing a separation **20/21** from the arom. derivative **22**. The two stereoisomers **20** and **21** could not be separated using ordinary CC: 665 mg of **20/21** (85%; GC: **20/21** 1:7) were obtained.

m) *Esterification* **21→23**. To a solution of 430 mg of **20/21/19** (obtained after repeated vitamin-B_{12}-catalyzed reduction of **19** and containing **21/20** in a 13:1 ratio) in 20 ml of CH_2Cl_2 and 1 ml of Et_3N, 539 mg of *p*-bromobenzoyl chloride and 40 mg of 4-(dimethylamino)pyridine were added. The mixture was stirred at r.t. for 18 h. After aq. extraction, the mixture was purified by chromatography (SiO_2, Et_2O/hexane). Prep. LC allowed the isolation of a mixture (195 mg) of *p*-bromobenzoates from the reduced alcohols **21/20** without contamination by the *p*-bromobenzoate from **19**. Crystals for X-ray analysis were grown from **23**/*p*-bromobenzoate of **20** using MeOH. A single crystal was split into two pieces. One piece was used for X-ray analysis, and the other was analyzed by capillary GC and shown to be devoid of the *p*-bromobenzoate of **20**. *2-(*cis*-4-(*tert*-Butyl)cyclohexyl)-2-methylpropyl* p-*bromobenzoate* (**23**): m.p. 83–84°, R_f 0.19 (Et_2O/hexane 1:20), t_R (GC, 50→300°) 40.0 min (no *trans*-isomer at 39.8 and *p*-bromobenzoate of **19** at 39.0 min). IR (KBr): 1713 (C=O); 1588, 1481 (arom. system); 1469, 1395, 1364, 1269, 966, 755. ^{1}H-NMR: 0.79 (*s*, 9H, $(CH_3)_3C$); 0.90 (*s*, 6H, $(CH_3)_2CCH_2O$); 0.95–1.6 (*m*, 6H, H–C(1), H–C(4), H_{ax}–C(2), H_{ax}–C(3), H_{ax}–C(5), H_{ax}–C(6)); 1.6–2.2 (*m*, 4H, H_{eq}–C(2), H_{eq}–C(3), H_{eq}–C(5), H_{eq}–C(6)); 4.01 (*s*, 2H, CH_2O); 7.5–7.55 (*m*, 2H, arom.); 7.78–7.86 (*m*, 2H, arom.). MS: 340/338 (1/1, $M^+ - (CH_3)_2CCH_2$), 257/255 (3/3), 202/200 (10/10, $BrC_6H_4COOH^+$), 194 (8, $M^+ - BrC_6H_4COOH$), 185/183 (42/44, $BrC_6H_4CO^+$), 157/155 (16/17, $BrC_6H_4^+$), 57 (100, $(CH_3)_3C^+$).

D. X-Ray Analyses of 6 and 23. – a) *Data of the Oxime* **6**.

Table 1. *Atom Coordinates (× 10^4) and Temperature factors ($Å^2$ × 10^3) of* **6**

Atom	*x*	*y*	*z*	U^a)
C(1)	3153(8)	890(2)	2893(7)	61(2)
C(2)	960(8)	1085(2)	2681(7)	66(2)
C(3)	258(8)	1313(2)	900(7)	66(2)
C(4)	1737(8)	1700(2)	490(7)	65(2)
C(5)	3845(9)	1481(2)	578(8)	80(2)
C(6)	4580(8)	1270(2)	2371(7)	78(2)
C(7)	3805(9)	724(2)	4770(7)	74(2)
C(8)	2345(11)	403(2)	5543(9)	109(3)
C(9)	5541(12)	844(3)	5724(10)	108(3)
C(10)	3340(8)	459(2)	1782(6)	63(2)
N(11)	1834(6)	243(1)	1008(5)	63(2)
O(12)	2356(6)	− 160(1)	116(5)	79(2)
C(13)	995(10)	1977(2)	− 1210(7)	73(2)
C(14)	897(12)	1675(3)	− 2817(7)	127(4)
C(15)	− 1107(12)	2181(3)	− 1151(10)	134(4)
C(16)	2422(12)	2380(3)	− 1404(10)	142(4)

[a]) Equivalent isotropic *U* defined as ⅓ of the trace of the orthogonalized U_{ij} tensor.

Table 2. *Bond lengths (Å) of* **6**

Bond	Length	Bond	Length
C(1)–C(2)	1.542(7)	C(1)–C(6)	1.527(8)
C(1)–C(7)	1.531(7)	C(1)–C(10)	1.509(7)
C(2)–C(3)	1.535(7)	C(3)–C(4)	1.534(7)
C(4)–C(5)	1.520(8)	C(4)–C(13)	1.553(7)
C(5)–C(6)	1.527(8)	C(7)–C(8)	1.512(9)
C(7)–C(9)	1.321(9)	C(10)–N(11)	1.250(6)
N(11)–O(12)	1.403(6)	C(13)–C(14)	1.505(8)
C(13)–C(15)	1.514(10)	C(13)–C(16)	1.506(10)

Table 3. *Bond Angles (deg.) of* **6**

Angle	Degrees	Angle	Degrees
C(2)–C(1)–C(6)	109.1(4)	C(2)–C(1)–C(7)	110.3(4)
C(6)–C(1)–C(7)	111.5(4)	C(2)–C(1)–C(10)	112.5(4)
C(6)–C(1)–C(10)	108.6(4)	C(7)–C(1)–C(10)	104.9(4)
C(1)–C(2)–C(3)	114.1(4)	C(2)–C(3)–C(4)	111.4(4)
C(3)–C(4)–C(5)	107.9(4)	C(3)–C(4)–C(13)	113.7(4)
C(5)–C(4)–C(13)	115.1(5)	C(4)–C(5)–C(6)	112.0(5)
C(1)–C(6)–C(5)	112.8(4)	C(1)–C(7)–C(8)	116.7(5)
C(1)–C(7)–C(9)	124.0(6)	C(8)–C(7)–C(9)	119.3(6)
C(1)–C(10)–N(11)	123.2(5)	C(10)–N(11)–O(12)	113.7(4)
C(4)–C(13)–C(14)	112.6(5)	C(4)–C(13)–C(15)	110.6(5)
C(14)–C(13)–C(15)	108.1(5)	C(4)–C(13)–C(16)	110.0(5)
C(14)–C(13)–C(16)	107.8(6)	C(15)–C(13)–C(16)	107.7(5)

b) *Data of the* p-*Bromobenzoate* **23.**

Table 4. *Atom Coordinates (× 10⁴) and Temperature Factors (Å² × 10³) of* **23**

Atom	*x*	*y*	*z*	*U*[a])
Br(1)	2319(2)	− 4074(1)	4694(1)	128(1)
C(1)	6924(18)	4258(8)	1983(6)	111(5)
C(2)	5666(24)	4767(12)	1350(9)	195(8)
C(3)	6769(36)	5899(15)	1006(11)	324(13)
C(4)	8526(18)	6610(9)	1421(5)	117(5)
C(5)	8403(42)	6502(15)	2230(8)	308(14)
C(6)	7684(26)	5306(11)	2595(7)	181(8)
C(7)	5822(14)	3068(8)	2352(5)	88(4)
C(8)	7342(15)	2550(10)	2917(6)	113(5)
O(9)	6312(10)	1414(6)	3232(4)	111(3)
C(10)	7512(14)	748(9)	3687(5)	81(4)
O(11)	9376(9)	1044(6)	3852(4)	115(3)
C(12)	6221(14)	− 394(8)	3935(5)	72(3)
C(13)	7158(14)	− 1184(8)	4434(5)	87(4)
C(14)	6016(17)	− 2266(8)	4664(6)	94(4)
C(15)	3918(14)	− 2576(8)	4387(5)	82(4)
C(16)	2981(16)	− 1816(10)	3899(6)	94(4)

Table 4 (continued)

Atom	x	y	z	U^{a})
C(17)	4119(13)	− 721(8)	3668(5)	89(4)
C(18)	5146(29)	2031(11)	1642(7)	208(9)
C(19)	3732(18)	3323(12)	2829(10)	199(9)
C(20)	9267(15)	7877(8)	1109(5)	98(4)
C(21)	7931(38)	8839(14)	1241(17)	358(18)
C(22)	11261(32)	8492(19)	1483(13)	345(15)
C(23)	9608(45)	7770(13)	223(8)	324(15)

[a]) Equivalent isotropic U defined as ⅓ of the trace of the orthogonalized U_{ij} tensor.

Table 5. *Bond Lengths (Å) of* **23**

Bond	Lengths	Bond	Lengths
Br(1)–C(15)	1.892(8)	C(1)–C(2)	1.452(18)
C(1)–C(6)	1.438(14)	C(1)–C(7)	1.543(13)
C(2)–C(3)	1.476(22)	C(3)–C(4)	1.389(22)
C(4)–C(5)	1.319(16)	C(4)–C(20)	1.502(13)
C(5)–C(6)	1.473(20)	C(7)–C(8)	1.480(14)
C(7)–C(18)	1.519(14)	C(7)–C(19)	1.538(15)
C(8)–O(9)	1.440(12)	O(9)–C(10)	1.330(11)
C(10)–O(11)	1.191(10)	C(10)–C(12)	1.470(12)
C(12)–C(13)	1.374(12)	C(12)–C(17)	1.373(11)
C(13)–C(14)	1.367(12)	C(14)–C(15)	1.373(13)
C(15)–C(16)	1.340(14)	C(16)–C(17)	1.378(13)
C(20)–C(21)	1.358(22)	C(20)–C(22)	1.440(21)
C(20)–C(23)	1.436(16)		

Table 6. *Bond Angles (deg.) of* **23**

Angle	Degrees	Angle	Degrees
C(2)–C(1)–C(6)	108.5(9)	C(2)–C(1)–C(7)	115.3(9)
C(6)–C(1)–C(7)	114.6(9)	C(1)–C(2)–C(3)	114.0(13)
C(2)–C(3)–C(4)	121.1(15)	C(3)–C(4)–C(5)	109.6(14)
C(3)–C(4)–C(20)	116.8(10)	C(5)–C(4)–C(20)	120.9(10)
C(4)–C(5)–C(6)	124.8(12)	C(1)–C(6)–C(5)	113.6(10)
C(1)–C(7)–C(8)	110.4(8)	C(1)–C(7)–C(18)	108.9(8)
C(8)–C(7)–C(18)	108.9(9)	C(1)–C(7)–C(19)	114.3(8)
C(8)–C(7)–C(19)	108.7(9)	C(18)–C(7)–C(19)	105.4(10)
C(7)–C(8)–O(9)	109.6(7)	C(8)–O(9)–C(10)	117.8(7)
O(9)–C(10)–O(11)	123.6(8)	O(9)–C(10)–C(12)	110.4(7)
O(11)–C(10)–C(12)	125.9(9)	C(10)–C(12)–C(13)	119.2(7)
C(10)–C(12)–C(17)	122.4(8)	C(13)–C(12)–C(17)	118.4(8)
C(12)–C(13)–C(14)	120.7(8)	C(13)–C(14)–C(15)	119.8(9)
Br(1)–C(15)–C(14)	120.4(7)	Br(1)–C(15)–C(16)	119.4(7)
C(14)–C(15)–C(16)	120.2(8)	C(15)–C(16)–C(17)	120.3(9)
C(12)–C(17)–C(16)	120.6(8)	C(4)–C(20)–C(21)	116.9(12)
C(4)–C(20)–C(22)	114.6(11)	C(21)–C(20)–C(22)	101.5(13)
C(4)–C(20)–C(23)	113.1(8)	C(21)–C(20)–C(23)	103.9(15)
C(22)–C(20)–C(23)	105.5(14)		

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