Tetrahedron. Vol. 28, pp. 5533 to 5541. Pergamon Press 1972. Printed in Great Britain

BASE INDUCED ISOMERIZATION OF γ,δ-EPOXYKETONES—III*

SYNTHESIS AND REACTIONS OF SOME NORCARANE DERIVATIVES

Y. GAONI

Department of Chemistry, The Weizmann Institute of Science, Rehovot, Israel

(*Received in the UK* 19 *April* 1972; *Accepted for publication* 19 *June* 1972)

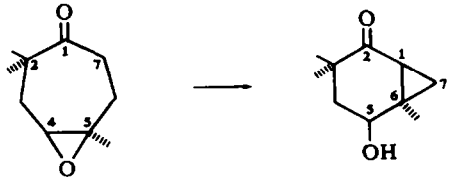
Abstract—Base treatment of epoxykarahanaenone (1) yields 5-*endo*-hydroxy-3,3,6-trimethylnorcarane-2-one (2). Dehydration of 2 with potassium hydrogen sulfate leads, partly, to [3.2.0]bicyclic ketones. Reaction of 2 with tosyl chloride in pyridine substitutes the 5-hydroxyl with chlorine; thionyl chloride in pyridine yields mainly bis-ethers of 2. Other reactions of 2 are described.

THE APPLICABILITY of the base-induced isomerization of epoxycarbonyl compounds to cyclic γ,δ-epoxyketones, leading to the formation of bicyclic compounds, has been demonstrated in the preceding paper[1a] with the synthesis of bicyclo [3.1.0]alkane derivatives of the thujane series.

Recent interest in reactions of 4-caren-2-ones[2,3] and their homologs[4,5] prompted us to apply the epoxyketone rearrangement to the synthesis of bicyclo[4.1.0]alken-2-one derivatives, the facile synthesis of karhanaenone[6] providing an easy approach to this system. The availability, though, of a variety of 4-cycloheptenones by other new methods[7,8] offers a wide choice of starting ketones and may lead to other derivatives of the carane system.

When epoxykarahanaenone (1), prepared by epoxidation of crude distilled karahanaenone[6] and purified by column chromatography, was treated with NaOEt in EtOH, it yielded stereospecifically one bicyclic hydroxyketone (2) in over 80% yield.

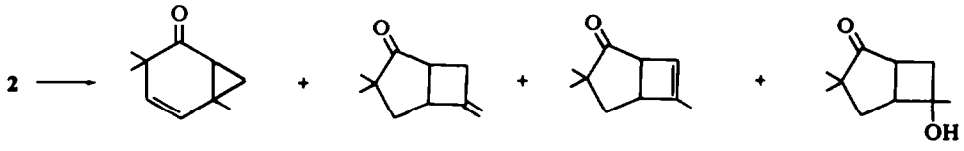
The assignment of an *endo* configuration to the hydroxyl in 2 (*cis*, or *syn*, to the cyclopropane) is based on the assumption of a backside displacement[9] of the epoxide-oxygen at C-5 by the anion created at C-7, with inversion at C-5. Models show that the methyl, while being inverted, remains *trans* to the hydroxyl at C-5 (in 2), the cyclopropane ring is consequently *cis* to this hydroxyl. Confirmation is obtained from the NMR spectrum of 2, where the C-5 *exo*-H appears as a double doublet at δ 4·20, an *endo*-H would be shielded by the cyclopropane by 0·4 to 1 ppm relative to that position (*cf.* ref. 11 and spectra of reduction products below).



1 2

* Part II, preceding communication.

Dehydration of **2** to a carenone could not be effected with *p*-TsOH in benzene.[1] The use of $KHSO_4$ at 170–180° yielded a mixture, mainly three unsaturated bicyclic ketones and one ketoalcohol. Two of the unsaturated ketones were isolated and identified as the desired norcarenone **3** (major component of the mixture) and the



3 **4** **5** **6**

rearranged product **4** (showing notably a cyclic 5-membered carbonyl absorption at 1740 cm^{-1} in the IR and a two-porton methylene broadened singlet at δ 4·83 in the NMR). The third unsaturated ketone was obtained in small quantity and was not completely purified; it was assigned structure **5** by analysis of its IR and NMR spectra.

When dehydration was stopped at a stage where no starting material remained, a hydroxyketone was also isolated, which was characterized as **6** through its spectral and analytical data. When this compound was submitted to dehydration by the same conditions as **2**, it yielded the same mixture of unsaturated ketones as that obtained from **2**, and in about the same relative proportions of *ca.* 8:2:1 (determined by VPC analysis) for **3**, **4** and **5** respectively.

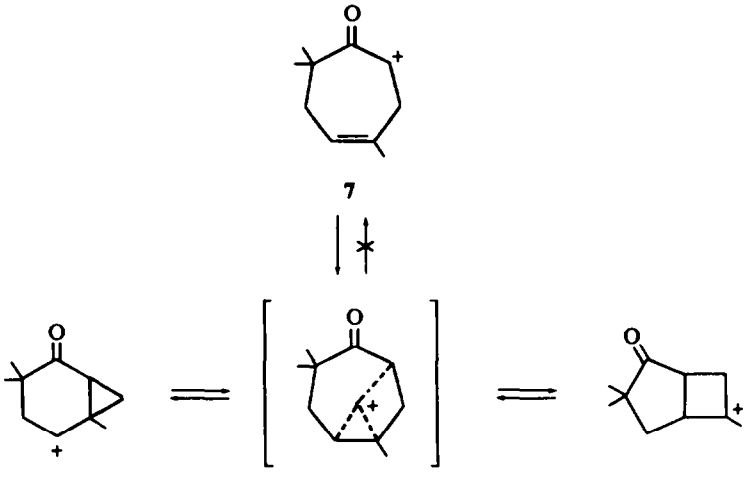
Formation of compounds **3** to **6** from **2** and of the same unsaturated ketones, **3** to **5**, from **6**, indicates a common intermediate, probably a non-classical cyclopropylcarbinyl cation, formulated as the three center carbonium ion **9**.[10*] In the non-equilibrating conditions of the dehydration, the kinetically controlled reaction[14] leads to products derived from intermediates **8** and **10** through loss of a proton or by reaction with unremoved water of dehydration. (Formation of the allylcarbinyl intermediate **7** is forbidden, as it would require build-up of a full positive charge next to the carbonyl; traces of what could be a dienone derived from **7** were, however, detected in a few chromatography fractions).

When the dehydration was carried out under reduced pressure, with simultaneous distillation of the reaction products, the formation of **6** was not observed, the other products were again obtained in the same relative proportions.

In those reactions of the ketoalcohol **2**, which involve displacement of the hydroxyl and formation of a carbonium ion in equilibrating conditions, no rearrangements are observed. This can be understood, considering that **7** cannot be formed and that **8** is more stable than **10**.[14]

When ketoalcohol **2** was reacted with *p*-TsOCl chloride in pyridine no tosylate was formed—the chlorides **11** and **12** were obtained instead, together with unchanged starting material. Displacement of a tosyloxy group by the chloride ion of pyridine hydrochloride had been used before for the conversion of alcohols to chlorides, but

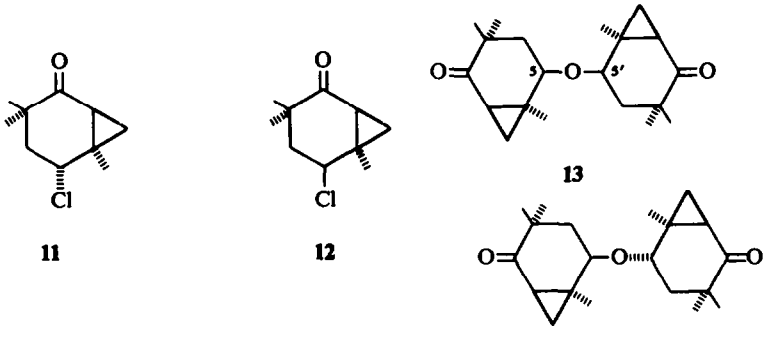
* This formulation does not have here the physical implication it has in the case of the unsubstituted cyclopropylcarbinyl cation,[10a] especially in view of the presence of an acyl substituent which must exert a strong influence on the structure of the ion. It seems, however, to be more convenient than the multiplicity of non-classical ionic structures proposed for cyclopropylcarbinyl derivatives,[11–14] in indicating clearly the three-way course in which it could evolve.



7 8 9 10

this occurred with inversion of configuration when applied to secondary tosyloxy groups.[15,16] The obtention in our case of both the *exo-* and *endo-chlorides* (**11** and **12**) suggests that the displacement is not of an S_N2 type, but rather an addition of the chloride ion to the stable intermediate carbonium ion **8**.

The same chloroketones **11** and **12** were obtained, in low yield, by the reaction of $SOCl_2$ in pyridine with the ketoalcohol **2**. The main products of this reaction were



11 12 13 14

the ethers **13** and **14**, resulting again from addition of the free alcohol **2** to the two faces of the carbonium ion **8**. Ethers **13** and **14** were identified through their mass and NMR spectra. The mass spectrum gave the molecular weight (318; $C_{20}H_{30}O_3$) and showed notably the two abundant ions of *m/e* 168 ($C_{10}H_{16}O_2$) and 151 ($C_{10}H_{15}O$) corresponding to the two halves of the molecule resulting from cleavage of a C—O ether bond (the former ion having picked-up a proton). The NMR spectrum was similar to that of the starting material **2**, except for a downfield shift of ~ 1 ppm for the low field proton. The difference in the splitting pattern of these protons allowed a configurational assignment to be made to the two ethers. In **13** only one double–doublet due to both the C-5 and C-5′ protons was observed, indicating a full equivalence of these protons; at the same time the two C-6 and C-6′ methyl signals coincided. In **14** two triplets

shifted by 0·18 ppm were observed for the same protons while the two methyls did not coincide. Since that ether bond which derives from the original alcohol **2** must be *endo*-oriented in both compounds, and *endo-endo*-configuration is assigned to **13** while a "non-equivalent" *endo-exo*-configuration is assigned to **14**.

The tentative configurational assignment of chlorides **11** and **12**, it is based mainly on the slight difference in the chemical shifts of the C-5 protons, the *endo*-protons of **11** being slightly more shielded by the cyclopropane ring relative to **12** (by ~0·2 ppm; smaller difference than for hydroxy-derivatives).

Some further support to this assignment may be provided by the results of the LAH reduction of **2** and **12**, both compounds leading similarly to the exclusive formation of an *exo*-OH at C-2. Thus reduction of the hydroxyketone **2** yielded exclusively one diol, 2-*exo*-5-*endo*-dihydroxy-3,3,6-trimethylnorcarane (**20**). The C-2 configuration was assigned on the basis of the chemical shift and splitting pattern of the C-2 proton, as compared to other 2-hydroxy compounds of the series (see below). This proton appeared as a singlet at δ 3·46, 0·56 ppm higher than the C-5 *exo*-H. The absence of coupling with the C-1 proton indicates a ~90° dihedral angle between the two protons. Models show that such an angle is conserved in the flipping half-chair conformation, expected for this system, with a C-2 *exo*-OH. With a C-2 *endo*-OH, or with other conformations, the angles measured are quite different and cannot account for a zero or near zero vicinal coupling constant.

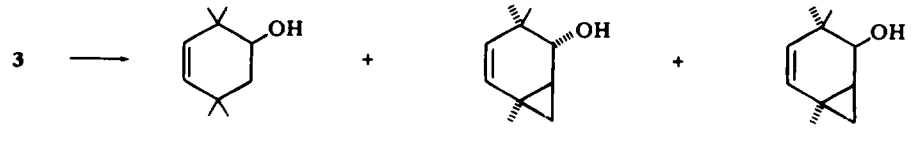
Reduction of ketone **12** with LAH also yielded one pure compound, *exo*-alcohol **15**, through hydrogenolysis of the chlorine. Here again the C-2 proton appeared as a singlet, at δ 3·23, suggesting an *endo*-configuration in a half-chair conformation. This configuration was confirmed by the obtention of **15** by a different route and comparison with the *endo*-alcohol **19** (see below).

Reduction of the isomeric chloroketone **11** by the same conditions yielded a mixture of several compounds, which was not analyzed.

The stereospecificity of reduction of both **2** and **12** must be related to the mechanism of reduction by the aluminium hydride; it probably involves coordination of the C-5 *endo*-oxygen or chlorine with the aluminium, with subsequent *endo* hydride addition at C-2.

Reaction of diol **20** with one mole of *p*-TsCl in pyridine did not yield any tosylate but gave a mixture of at least ten compounds (VPC) which were not separated or identified.

A different set of reactions of the carane system concerns the cyclopropane ring. When carone and carenone systems are reacted with reagents which attack cyclopropyl ketones, the products are shown to be controlled by stereo-electronic factors, which may outweigh thermodynamic factors. In particular, the reductive cleavage of both the saturated[17] and unsaturated[3] ketones break that bond which has maximum overlap with the π-system of the carbonyl (i.e., the 1,7-bond of both systems). When ketone **3** was submitted to such a reduction (Na in EtOH) a unique cleavage

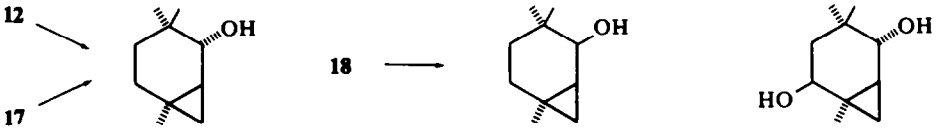


16 **17** **18**

product, **16**, was indeed obtained, resulting from breaking of the same 1,7-bond. Alcohol **16** constituted 60% of the mixture and was accompanied by the normal reduction products of **3**, namely, the *exo*- and *endo*-alcohols **17** and **18** (12 and 28% of the mixture).

Alcohol **16** was identified by LAH reduction of the corresponding ketone, 2,2,5,5-tetramethyl-3-cyclohexanone.[18] This structural proof also supports the structure of ketone **3**.

Alcohols **17** and **18** were identified by LAH reduction of **3**, which mainly yielded the same two alcohols, and in about the same ratio, 3:7, as the Na-EtOH reduction (a very similar ratio of *exo*- to *endo*-alcohols was obtained by Bellamy and Whitham[3] in the reduction of 3-methylcarenone). The two alcohols were separately reduced over 5% Pt/C to the saturated bicyclic alcohols **15** and **19**.*



15 **19** **20**

The configurations of the unsaturated and saturated alcohols could now be established by comparison of their NMR spectra, considering particularly the chemical shift of the C-2 proton. In agreement with Poulter *et al.*[11] an *endo*-configuration was assigned to the shielded C-2 protons in **17** and **15**; these resonated at higher field (0·4 to 0·6 ppm) than the corresponding protons in the respectively isomeric **18** and **19**, which were therefore assigned an *exo*-configuration (*endo*-OH).

EXPERIMENTAL

M.ps are uncorrected. IR spectra were recorded on a Perkin–Elmer spectrophotometer. Infracord Model 137. NMR spectra were recorded on a Varian A-60 spectrometer. Mass spectra were determined on an Atlas CH-4 spectrometer. VPC analysis or preparative separations were carried out on an Aerograph A-700 instrument, with columns of 6% FFAP or 10% DC-710 on Chromosorb W, 5 or 10 feet long.

Epoxykarahanaenone (2,2,5-*trimethyl*-4-*cycloheptenone epoxide*, **1**). Crude distilled karahanaenone[6] (14 g; containing *ca.* 60% of the ketone by VPC) was epoxidized with *m*-chloroperbenzoic acid (18·2 g) in CH_2Cl_2 (200 ml), with ice cooling. The crude epoxide was chromatographed on Florisil (250 g), fractions being monitored by VPC (DC-710, 130°). Elution with 5% ether in hexane yielded 6·4 g of 95% pure product and 2·5 g of less pure material. The purest fractions were combined and distilled, yielding pure **1**, b.p. 130–140° (bath temperature)/1 mm; $\nu_{max}^{CCl_4}$ 1704, 1450, 1100, 1085 cm^{-1}. δ (CCl_4) 1·05 (6H, s, *gem*-dimethyl), 1·25 (3H, s, C-5 methyl), 1·8–2·6 (6H, m, ring-methylenes), 2·85 (1H, t, J = 6·0 Hz, C-4 H) (Found: C 71·15, H, 9·46. $C_{10}H_{16}O_2$ requires: C, 71·39; H, 9·59%).

5-endo-*Hydroxy*-3,3,6-*trimethylnorcaran*-2-*one* (**2**). (a) The epoxide **1** (8 g) was refluxed in EtOH with NaOEt (from 1·2 g Na in 50 ml EtOH) for 15 min. Most of the EtOH was evaporated at reduced pressure and the residue taken in ether and washed with sat NaCl aq. VPC showed the absence of starting material and the formation of only one product. Evaporation of the ether yielded a gum. Trituration with cold pentane and cristallization from pentane ether yielded 5·6 g (70%) of **2**. m.p. 80–81°; $\nu_{max}^{CCl_4}$ 3450, 1683, 1213, 1078, 1046, 1024 cm^{-1}. δ ($CDCl_3$) 0·82 (1H, dd, C-7 *exo*-H†; $J_{1,7}$ 7, J_{gem} 10 Hz), 1·05 (6H, s, two methyls), 1·30 (3H, s, methyl), 1·25–2·0 (4H, m,), 4·20 (1H, dd, C-5 *exo*-H; $J_{5,6}$ 6, $J_{5,trans\text{-}4}$ 11 Hz), 2·20 (1H, s, OH) (Found: C, 71·50; H, 9·30. $C_{10}H_{16}O_2$ requires: C, 71·39; H, 9·59%). (b) To 10 g of epoxide **1** in 60 ml EtOH

* While **18** was neatly reduced, **17** gave a 1:1 mixture of **15** with an unidentified product—probably a cycloheptanol—which showed no absorption at high field (zero to 0·8 ppm) in the NMR.

† The assignment of the highest field resonance to the *exo*-cyclopropyl C-7 proton is in accord with both Dauben and Todd Wipke[19] and Agami and Prevost.[20]

were added 50 ml of 1N NaOH and the solution refluxed for 15 min. Most of the EtOH was evaporated at reduced pressure and the remaining solution saturated with K_2CO_3 and ether extracted, yielding 9·2 g of crude solidified **2**. Cristallization (pentane-ether) yielded 7·2 g (72%) of **2**, m.p. 79–81°.

Chromatography of combined mother-liquors yielded more of **2**, raising the average yield to 80–85%.

Dehydration of hydroxy-ketone **2**. (a) A mixture of compound **2** (6 g) with 6 g of fused powdered $KHSO_4$ was warmed in an oil-bath, under N_2, at 170–180° until no more starting material was observed on VPC (DC-710, 5 feet, 140°), which then showed mainly two peaks in a ratio of *ca.* 5:3. A different column (FFAP, 10 feet, 150°) then incompletely resolved the above first eluted peak into three, in a ratio of *ca.* 1:2:8, by order of elution.

Ether was added to the cooled mixture which was dried (Na_2SO_4) and filtered. Chromatography of the residue (5·2 g) obtained upon evaporation of ether, on Florisil (150 g), yielded first (by elution with 2 and 5% ether in hexane) a mixture of ketones (1·24 g) then 0·90 g of 3,3,6-*trimethyl*-4-*hicyclo* [4.1.0]*hepten*-2-*one*, (3,3,6-*trimethyl*-4-*norcarene*-2-*one*(**3**) as an oil, b.p. 110° (bath temperature)/20 mm; $\nu_{max}^{CCl_4}$ 1683, 1292, 1216, 1185, 1147, 1088, 1071, 910, 882 cm^{-1}. $\delta(CCl_4)$ 1·05 (6H, s, two methyls), 1·28 (3H, s, methyl), *ca*, 1·1–1·30 (1H, m) and 1·58–2·0 (2H, m, cyclopropane protons), 5·2 d and 5·8 d (2H. AB pattern, $J_{4,5}$ 10 Hz vinylic protons). Molecular weight *m/e*. 150 (M^+) 135, 122, 107, 91). (Found: C, 79·72; H, 9·10. $C_{10}H_{14}O$ requires: C, 79·96; H, 9·39%). *Semi-carbazone*, m.p. 151–152° (hexane) (Found: C, 64·20; H, 8·45; N, 20·00. $C_{11}H_{17}N_3O$ requires: C, 63·74; H, 8·27; N, 20·27%). Mass spectrum *m/e* 207 (M^+). Further elution, with ether–hexane 1:4, yielded 1·2 g of 6-*hydroxy*-3,3,6-*trimethylbicyclo*[3.2.0]*heptan*-2-*one* (**6**) as a distillable oil, b.p. (bath temperature) 170°/20 mm. $\nu_{max}^{CCl_4}$ 3370, 1730, 1226, 958 cm^{-1}. δ (CCl_4) 0·98 s and 1·13 s (6H, two methyls), 1·43 (3H, s, methyl), 1·75–2·85 (6H, m), 3·10 (1H, s, OH). Mass spectrum *m/e* 168 (M^+), 153, 150, 135, 125, 111, 107. (Found: C, 70·89, H, 9·56. $C_{10}H_{16}O_2$ requires: C, 71·39; H, 9·59%). *Semi-carbazone*, mp. 216° (EtOH) (Found: C, 59·22; H, 5·56; N, 18·86. $C_{11}H_{19}N_3O_2$ requires: C, 58·64; H, 8·50; N, 18·65%). Mass spectrum *m/e* 225 (M^+).

Further elution, with ether, yielded unidentified viscous oils (1·5 g). Rechromatography of the first-eluted ketone mixture (1·24 g) on Kieselgel yielded first 190 mg of a pure compound (the second eluted on VPC, FFAP column), identified as the 3,3-*dimethyl*-6-*methylenebicyclo*[3.2.0]*heptan*-2-*one* (**4**), b.p. 110° (bath temperature)/20 mm; $\nu_{max}^{CCl_4}$ 1740, 890 cm^{-1}. δ (CCl_4) 1·00 s and 1·12 s (6H, two methyls), 1·5–3·5 (6H, m), 4·83 (2H, s, br, $C=CH_2$). Mass spectrum *m/e* 150 (M^+), 135, 122, 107, 94·91. (Found: C, 79·40; H, 9·35. $C_{10}H_{14}O$ requires: C, 79·96; C, 9·39%). *Semi-carbazone*, m.p. 191° (Found: C, 63·65; H, 7·99; N, 20·39. $C_{11}H_{17}N_3O$ requires: C, 63·74; H, 8·27; N, 20·27%). Mass spectrum *m/e* 207 (M^+).

Further elution yielded mixed fractions, then some which were 95% pure in one compound (the first eluted on VPC) tentatively identified as 3,3,6-trimethyl-6-bicyclo[3.2.0]hepten-2-one (**5**), $\nu_{CCl_4}^{max}$ 1735, 1640 (w), 1130, 1110, 1086 cm^{-1}. δ (CCl_4) 1·0 s and 1·15 s (two methyls), 1·75 (s, br, vinylic methyl) 2·7–3·2 (3H, m), 5·75 (s, br, vinylic H). These were followed by mixtures of **5** with minor impurities, showing notably a carbonyl absorption at 1670 cm^{-1} in the IR and vinylic protons in the NMR. Still further elution yielded ketone **3** (0·42 g).

(b) Dehydration of **2** (2·6 g), with $KHSO_4$ (2·6 g) was carried out in a bath at 220° under 60 mm pressure in a short path distillation apparatus, and was continued until most of the material had distilled over. The distillate was taken-up in ether and dried yielding 1·5 g of oil, after solvent evaporation. The residue was also extracted with ether, yielding 0·84 g. VPC analysis of the distillate showed the formation of the unsaturated ketones in the same relative ratio as above; the peak of the hydroxy ketone **6** was not observed (FFAP). Chromatographic separation on Kieselgel yielded the same unsaturated ketones **3**, **4** and **5** as above. VPC analysis of the residue showed that it contained more of the ketone mixture, plus unidentified heavier material.

Dehydration of the hydroxyketone **6**. Dehydration of 0·8 g of **6** was carried out by method (a) above. VPC analysis showed the formation of the same mixture of compounds and in the same proportion as above, except for **6** which had disappeared. The unsaturated ketones were separated and identified as already described.

Reduction of ketone **3**. (a) *With* Na *in* EtOH. Cut Na (2·0 g) was added to a refluxing solution of **3** (0·8 g) in absolute EtOH (20 ml) and reflux was continued for ½ h. Work-up yielded 0·74 g of a three component mixture, in the proportions of 60, 12 and 28%, by order of elution on VPC (DC-710, 90°). Chromatography on Kieselgel (30 g) and elution with 5% and 10% ether in hexane effected a partial separation of the major component, identical in all respects with the alcohol **16** (below). This was followed by the *exo*-bicyclic alcohol **17** and the *endo*-bicyclic alcohol **18** (second and third eluted on VPC). Alcohols **17** and **18** were identical in all respects with the reduction products of ketone **3** with LAH (below).

(b) *With lithium aluminium hydride.* Ketone **3** (0·45 g) in ether (15 ml) was added to LAH (0·23 g) in 20 ml of ether, and the total refluxed for 15 min. After decomposition (EtOAc then sat. Na_2SO_4 aq), filtration and drying (K_2CO_3), the crude material showed two close peaks on VPC (DC-710, 100°), in a ratio of *ca* 3:7. Chromatographic separation (Kieselgel, 50 g) yielded first 62 mg of the minor component then 118 mg of mixed fractions and finally 192 mg of the second component, all eluted with 6% ether in hexane. The first material was distilled (bulb-to-bulb) to yield pure 2-exo-*hydroxy*-3,3,6-*trimethyl*-4-*norcarene* (**17**), b.p. 100–110° (bath temperature)/20 mm, $\nu_{max}^{CCl_4}$ 3350, 1066, 1026 cm^{-1}. δ (CCl_4), 0·34 t and *ca.* 0·75–1·1 (3H, cyclopropyl protons), 0·96 s, 1·0 s and 1·17 s (three methyls), 2·40 (1H, s, OH), 3·23 (1H, d, *J* 3·5 Hz, C-2 *endo*-H), 5·30 d and 5·67 d (2H, AB pattern, *J* 9·5 Hz, vinylic protons). (Found: C, 78·60; H, 10·41. $C_{10}H_{16}O$ requires: C, 78·89; H, 10·59%). Material from pure fractions of the second component was also distilled, b.p. 110–115° (bath temperature)/20 mm, and the distillate then solidified. It was recrystallized from pentane and identified as 2-endo-*hydroxy*-3,3,6-*trimethyl*-4-*norcarene* (**18**), m.p. 40–41°, $\nu_{max}^{CCl_4}$ 3400, 1069, 1021 cm^{-1}. δ (CCl_4) 0·4-*ca.* 1·4 (resolved m, partly under methyls, cyclo-propyl protons), 0·92 s, 1·03s and 1·18 s (three methyls), 2·15 (1H, s, OH), 3·88 (1H, d, *J* 5·5 Hz, C-2 *exo*-H), 5·10 d and 5·60 d (2H, AB pattern, *J* 10 Hz, vinylic protons) (Found: C, 78·65; H, 10·51. $C_{10}H_{16}O$ requires: C, 78·89; H, 10·19%).

2,2,5,5-*Tetramethyl*-3-*cyclohexen*-1-*ol* (**16**). 2,2,5,5-Tetramethyl-3-cyclohexen-1-one[18] (220 mg) was reduced in ether with 100 mg of LAH, by 15 min reflux. The usual work-up yielded 170 mg of alcohol **16** as an oil, b.p. 110–120° (bath temperature)/20 mm, which then solidified, m.p. 42–44° (lit. [21]: 44–45°). δ (CCl_4) 0·88 s, 1·0 s and 1·03 s (four methyls), 1·53 (d, 2H, *J* 7·5 Hz, —CH_2—), 3·65 [t, (after addition of D_2O), 1H, *J* 7·5 Hz, —C<u>H</u>(OH)]; before addition of D_2O, the hydroxyl proton appeared as a doublet at δ 2·45 (*J* 6 Hz) and the low-field proton as a broadened quartet (superimposed double triplet), indicating a slow exchange on the highly hindeted hydroxyl.

2-endo-*Hydroxy*-3,3,5-*trimethylnorcarane* (**19**). Recrystallized unsaturated alcohol **18** (80 mg) was reduced in EtOAc (15 ml) with 5% Pt/C catalyst (60 mg), at atmospheric pressure, until the uptake of hydrogen had ceased (22·5 ml H_2). VPC (DC-710) showed the formation of only one compound and the absence of starting material. The recovered substance was distilled to yield pure **19**, b.p. 75° (bath temperature)/0·5 mm $\nu_{max}^{CCl_4}$ 3470, 1242, 1104, 1083, 1048, 1030, 1008, 980, 960 cm^{-1}. δ (CCl_4) 0·80 s (2 methyls), 1·07 s (methyl), 0·15 (1H, dd, $J_{1,exo\text{-}7}$ 9·0, $J_{exo\text{-}7,endo\text{-}7}$ 4·5 Hz, C-7 *exo*-H), 0·53 (1H, t, $J_{1,endo\text{-}7}$ 4·5, $J_{exo\text{-}7,endo\text{-}7}$ 4·5 Hz, C-7 *endo*-H), *ca.* 0·8 to 2·0 (5H, m,), 3·62 (1H, d, $J_{1,exo\text{-}2}$ 8·0 Hz, C-2 *exo*-H). (Chemical shifts and coupling constants of the C-7 protons in accord with Dauben[19]) (Found: C, 77·60; H, 11·73. $C_{10}H_{18}O$ requires: C, 77·86; H, 11·76%).

Catalytic hydrogenation of the unsaturated alcohol **17**. Distilled alcohol **17** (40 mg) was reduced in EtOAc (10 ml) with 5% Pt/C (40 mg); 17·7 ml H_2 were absorbed in 3 hr. VPC (DC-710) showed the formation of two products in a 1:1 ratio and TLC showed the absence of starting material. The NMR spectrum of the total reduced material showed the formation of **15** (below) with additional peaks, mainly in the methyl-region, but none in 0–0·8 region or at 3·63 (due to **19**). A rough separation was achieved by filtration of the mixture, in benzene, on 3 g of Florisil, with monitoring by VPC. The best fractions still contained the unknown compound but the IR spectrum was identical with that of pure **15** while the NMR spectrum was mainly that of **15**.

Reaction of ketoalcohol **2** *with* p-*toluenesulfonyl chloride in pyridine. Chlorides* **11** *and* **12**. The ketoalcohol **2** (3·3 g) was reacted in pyridine (20 ml) with 4·0 g of TsCl, overnight at room temperature. Water was added and the mixture extracted. The extracts were washed with water, dilute HCl, $NaHCO_3$ aq, and sat. NaCl aq. Evaporation of ether yielded 2·3 g of an oily mixture of three compounds (VPC, DC-710), the main being the starting material **2**. (The water layer was saturated with NaCl and ether extracted, yielding 0·55 g of almost pure **2**).

Chromatography of the oily extract on Kieselgel (120 g) separated first a solid (0·1 g, eluted with ether-hexane 1:4) identified as 5-exo-*chloro*-3,3,6-*trimethyl*-*norcarane*-2-*one* (**11**), m.p. 65–66° (pentane). $\nu_{max}^{CCl_4}$ 1694, 1216, 1145, 917, 870 cm^{-1}, δ (CCl_4) 1·03 (s, two methyls), 1·37 (s, methyl), 0·8–2·0 (5H, m), 4·40 (1H, dd, J_1 7, J_2 10·5 Hz, C-5 *endo*-H) (Found: C, 64·58; H, 7·92. $C_{10}H_{15}C10$ requires: C, 64·34; H, 8·10%).

The second substance (0·6 g, eluted with same solvent mixture) was obtained as an oil which was distilled but later solidified. It was identified as 5-endo-*chloro*-3,3,6-*trimethylnorcarane*-2-*one* (**12**), m.p. 43–44° (pentane). $\nu_{max}^{CCl_4}$ 1694, 1231, 1209, 1152, 1128, 935, 909 cm^{-1}. δ /CCl_4) 1·05 s, 1·26 s and 1·37 s (three methyls), 0·95–1·0 (m, 3H), 2·12 (2H, d, *J* 3 Hz, C-4 —CH_2—), 4·59 (1H, t, *J* 3 Hz, C-5 *exo*-H). Mass spectrum *m/e* 188, 186 (M^+) (Found: C, 64·10; H, 8·12. $C_{10}H_{15}C10$ requires: C, 64·34; H, 8·10%. Elution with ether-hexane 3:2 yielded 1·3 g of recovered ketone **2**.

Reaction of ketoalcohol **2** *with* $SOCl_2$ *in pyridine. Ethers* **13** *and* **14**. Ketoalcohol **2** (1·0 g) was reacted in

pyridine (6 ml) at room temp with 0·5 ml $SOCl_2$. Work-up after ½ hr as above yielded a mixture which was chromatographed on Kieselgel (60 g). Chlorides **11** and **12** were first isolated and identified by direct comparison (m.p. and IR) with the authentic chlorides. Elution with ether-hexane 1:1 then yielded solid fractions of variable m.ps (mixtures) but with hardly any variation in IR or NMR. These recombined mixed fractions (0·62 g) were crystallized first from ether, yielding a few mg of an almost pure isomer, then chromatographed on neutral alumina (activity II, 60 g). Elution with ether hexane (1:2) achieved a partial separation of two isomeric compounds.

The first compound was obtained as heavy prisms (from pentane), mp.. 117–118°, and identified as the *bis-5,5'-endo*-ether **13**, ν_{max}^{KBr} 1683, 1190, 950, 902, 901, 840, 810, 772 cm^{-1}. δ ($CDCl_3$) 1·08 and 1·12 (two partly resolved methyl signals representing four methyl groups), 1·28 (s, two methyls), 0·8–2·0 m, 5·10 (dd, J 7, J' 11 Hz, C-5 and C-5' protons). Mass spectrum *m/e* 318 (M^+), 168, 151, 123. (Found: C, 75·19; H, 9·43. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%).

The second compound was obtained as fine needles from pentane or pentane-ether, m.p. 110–111°, resolidifying to melt at 122–123°, or as plates from ether or EtOH, m.p. 122–123°. It was identified as the *5-endo-5'-exo-ether* **14**. ν_{max}^{KBr} 1683, 1200, 950, 920, 895, 840, 799, 778 cm^{-1}. δ ($CDCl_3$) 1·08 and 1·12 (two partly resolved methyl signals representing four methyls), 1·30 s and 1·33 s (two methyls), 0·85–2·0 m, 5·04 t and 5·22 t (J 7·5 Hz, C-5 *exo*-H and C-5' *endo*-H). Mass spectrum *m/e* 318 (M^+), 168, 151 and 123. (Found: C, 75·25; H, 9·42. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%). (This second substance was identical to the small amount of material obtained by direct crystallization from ether, m.p. 122–123° from EtOH).

Reduction of chloroketone **12** *with lithium aluminium hydride.* Ketone **12** (165 mg) was reduced in ether (15 ml) with LAH (90 mg) at reflux for 20 min. VPC and TLC showed the formation of one compound and the absence of starting material. Distillation of the crude product, b.p. 80° (bath temperature)/1 mm, yielded pure 2-exo-*hydroxy*-3,3,6-*trimethylnorcarane* (**15**). $\nu_{max}^{CCl_4}$ 3450, 1088, 1039, 1018 cm^{-1}. δ (CCl_4) 0·80 s, 0·87 s and 1·08 s (three methyls), 0·0–0·75 (3H, m, ABC second order pattern, cyclopropyl protons), *ca.* 0·9–1·3 m and 1·45–1·8 m (4H), 2·50 (1Y, s, OH), 3·20 (1H, s, C-2 *endo*-H) (Found: C, 77·47; H, 11·32. $C_{10}H_{18}O$ requires: C, 77·86; H, 11·76%). When ketone **11** was similarly reduced, it yielded a mixture of compounds which was not fractionated. NMR showed the presence of **15** and absence of **19**.

Reduction of hydroxyketone **2** *with lithium aluminium hydride.* Ketone **2** (2 g) in ether (50 ml) was added dropwise, during 30 min, to LAH (0·5 g) in ether (150 ml), causing reflux of ether. After additional 15 min at room temp, no starting material was present. The usual work-up yielded 1·8 g of a solid which was recrystallized from benzene to yield pure 2-exo-5-endo-*dihydroxy*-3,3,6-*trimethylnorcarane* (**20**). m.p. 122–123°. ν_{max}^{KBr} 3260, 1087, 1037, 1013, 987 cm^{-1}. δ ($CDCl_3$) 0·90 (s, two methyls), 1·25 (s, methyl), 0·3–1·0 (m, 4H, cyclopropyl protons and one C-4 H), 1·57 (1H, q, lower part of a doubly split AB pattern, $J_{4,4'}$ 14, $J_{4',5}$ 6·5 Hz, C-4' H), 3·46 (1H, s, C-2 *endo*-H), 4·02 (1H, dd, C-5 *exo*-H; $J_{4,5}$ 12, $J_{4',5}$ 6·5 Hz) 1·80 (s, br, two OH, exchangeable with D_2O) (Found: C, 70·70; H, 10·55. $C_{10}H_{18}O_2$ requires: C, 70·54; H, 10·66%).

Reaction of diol **20** *with* p-*toluenesulfonylchloride in pyridine.* Diol **20** (0·7 g) in pyridine (5 ml) was treated with *p*-TsCl (0·8 g) overnight at room temp. Work-up, as for **2** above, yielded 0·4 g of an oily mixture of several compounds (VPC, DC-710, 120°) which were not fractionated. No tosyloxy derivative was detected in the NMR spectrum.

Acknowledgement—The author thanks Mrs. N. Shoef for skillful experimental assistance in this and the preceding work[1].

REFERENCES

[1] [a] Y. Gaoni, *Tetrahedron* **28**, 5525 (1972); [b] Y. Gaoni, *Israel J. Chem.* **9**, 63 (1972)

[2] J. E. Baldwin and S. M. Krueger, *J. Am. Chem. Soc.* **91**, 2396 (1969)

[3] A. J. Bellamy and G. H. Whitham, *Tetrahedron* **24**, 247 (1968)

[4] L. A. Paquette, R. E. Eizember and O. Cox, *J. Am. Chem. Soc.* **90**, 5153 (1968)

[5] L. A. Paquette, G. V. Meehan and R. E. Eizember, *Tetrahedron Letters* 995 (1969)

[6] E. Demole and P. Enggist, *Helv. Chim. Acta* **54**, 456 (1971)

[7] S. J. Rhoads and C. F. Brandenburg, *J. Am. Chem. Soc.* **93**, 5805 (1971)

[8] R. Noyory, S. Makino and H. Takaya, *Ibid.* **93**, 1272 (1971)

[9] N. A. Nelson and G. A. Mortimer, *J. Org. Chem.* **22**, 1146 (1957)

[10] [a] G. A. Olah, C. L. Jenell, D. P. Kelly and R. D. Proter, *J. Am. Chem. Soc.* **94**, 146 (1972); [b] G. A. Olah, *Ibid.* **94**, 808 (1972)

[11] C. D. Poulter, E. C. Friedrich and S. Winstein, *J. Am. Chem. Soc.* **92**, 4274 (1970)
[12] P. Schleyer and V. Buss, *Ibid.* **91**, 5880 (1969)
[13] W. R. Dolbier, *Mechanisms of Molecular Migrations*, B. S. Thyagarajan Ed., Vol. 3, p. 22 Wiley-Interscience, (1971)
[14] M. Hanack and H. J. Schneider, *Angewan. Chem., Intern. Ed.* **6**, 666 (1967)
[15] F. C. Chang, R. T. Blickenstaff, A. Feldstein, J. R. Gray, G. S. McCaleb and D. H. Sprunt, *J. Am. Chem. Soc.* **79**, 2164 (1957)
[16] R. T. Blickenstaff and F. C. Chang, *Ibid.* **80**, 2726 (1958)
[17] W. G. Dauben and E. J. Deviny, *J. Org. Chem.* **31**, 3749 (1966)
[18] Y. Gaoni and E. Wenkert, *Ibid.* **31**, 3809 (1966)
[19] W. G. Dauben and W. Todd Wipke, *Ibid.* **32**, 2976 (1967)
[20] C. Agami and C. Prévost, *Bull. Soc. Chim. Fr.* 2299 (1967)
[21] A. W. Allan, R. P. A. Sneeden and J. M. Wilson, *J. Chem. Soc.* 2186 (1959)