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# CHEMISTRY OF STRAINED POLYCYCLIC COMPOUNDS—IX[1]

## THE SYNTHESIS AND HOMOKETONIZATION OF 4-SUBSTITUTED HOMOCUNEANE ACETATES

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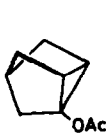
**Abstract**—The synthesis of three bridgehead homocuneanes acetates viz 1-bromopentacyclo [4.3.0.0$^{2,4}$.0$^{3,8}$.0$^{5,7}$]nonan-9-one ethylene ketal 4-acetate (**10**), 1-bromopentacyclo[4.3.0.0$^{2,4}$.0$^{3,8}$.0$^{5,7}$]nonane 4-acetate (**22**) and pentacyclo[4.3.0.0$^{2,4}$.0$^{3,8}$.0$^{5,7}$]nonan-9-one ethylene ketal 4-acetate (**31**) is described, starting from the readely available homocubane carboxylic acid (**4**). The base and acid catalyzed homoketonization reaction of these acetates has been studied. Under basic conditions the acetates (**10**, **22** and **31**) are converted into tetracyclo[4.3.0.0$^{2,4}$.0$^{3,8}$]nonane derivatives by a cyclopropanol ring cleavage. This homoketonization reaction is a stereospecific process proceeding with *retention* of configuration. The effect of cage strain on the stereochemistry of base induced homoketonization of bridgehead cage alcohols is discussed.

The acid catalyzed homoketonization of acetate (**10**) was also found to occur exclusively with retention of configuration.

Base catalyzed electrophilic substitution on saturated carbon with carbon as leaving group (SE-reaction) has been systematically studied in open chain systems.[2] The stereochemical course of this reaction is strongly dependent on the nature of the solvent, e.g. inversion of configuration (with respect to carbon as leaving group) in solvents of high dissociating power capable of donating protons, and retention of configuration in low dielectric nondissociating solvents. In cyclic systems in which the CO leaving group remains in the same molecule, structural effects seem to be more important than solvent effects in governing the stereochemical course of the SE-reaction.[3] This has been elegantly demonstrated by Nickon *et al.*[4] for the homoketonization of 1-acetoxynortricyclane **1** and 2-acetoxytriaxane **2**. Both in polar and non-polar media the cyclopropanol ring opening in these polycyclic structures proceeds almost exclusively with *inversion* of configuration.

The base induced homoketonization of strained polycyclic bridgehead alcohols in which the bridgehead is being flanked by 4-[5] and/or 5-[6]membered rings has actively been investigated in recent years. It was found that in these structures homoketonization proceeds with exclusive *retention* of configuration independent of the solvent, which is in contrast with the *inversion* observed for the aforementioned cyclopropanol containing polycyclic compounds.

The bridgehead polycyclic alcohols, containing cyclobutanol and/or cyclopentanol rings, which were studied in this context, show quite a diversity, viz. homocubanols, 1,3-bishomocubanols, birdcage alcohol, tricyclo[3.2.0.0$^{2,6}$]heptanol and tricyclo[3.3.0.0$^{3,7}$]octanol.

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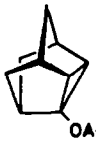


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3

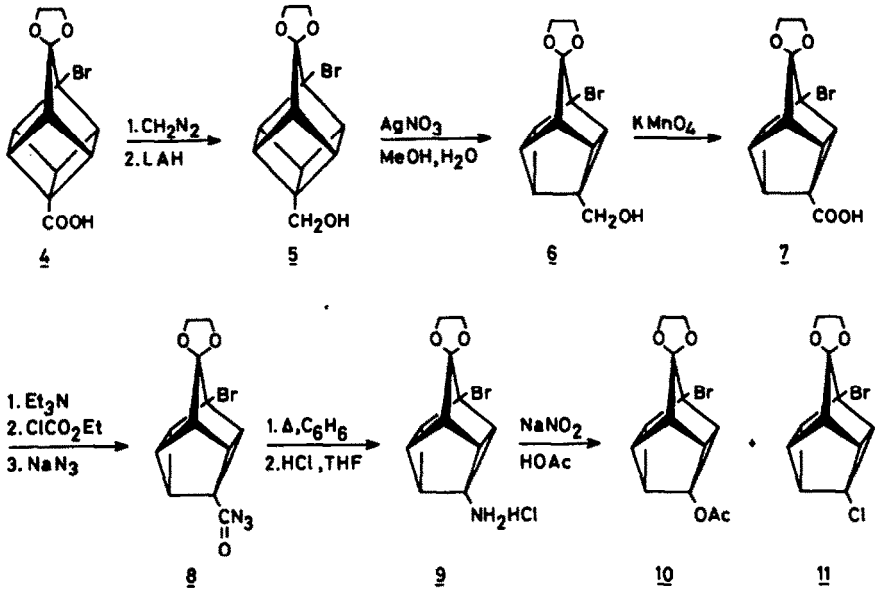
However, the cyclopropanol containing systems, studied so far, are limited to two rather related structures. Therefore, we figured that inversion of configuration observed for Nickon's nortricyclane and triaxane system, may not be a general feature for the base induced ring opening of cyclopropanols constrained in a polycyclic structure, but instead may be typically associated with these substrates.

Consequently, we decided to study the SE-type reaction in the homocuneane cage system **3** in which a cyclopropanol is incorporated in a polycyclic structure related to triaxane but which is considerably more strained.

In design our synthetic approach to the homocuneane nucleus was based upon the Ag(I)-catalyzed cage transformation[7] of the homocubane skeleton. 1-Bromohomocubane-4-carboxylic acid **4** was chosen as the starting material as it is readily available in large quantities.[8] Its transformation into the desired 4-homocuneane acetate **10** is outlined in Scheme 1.

Attempts to prepare homocuneane carboxylic acid **7** by direct isomerization of **4** or its methyl ester with either $AgNO_3$ in MeOH/$H_2O$ or $AgClO_4$ in benzene were unsuccessful. After refluxing for 24 hr, no trace of the desired homocuneane derivative could be detected. To circumvent this problem, the acid **4** was reduced to the homocubane methylalcohol **5** which was treated with $AgNO_3$ in MeOH/$H_2O$. A rapid and quantitative isomerization to homocuneane methylalcohol **6** was accomplished. Oxidation of **6** with $KMnO_4$ under two phase conditions[9] afforded homocuneane carboxylic acid **7** in an overall yield of 60%.

Transformation of carboxylic acid **7** into acetate **10** was achieved by conversion of **7** to carbonylazide **8**, subsequent Curtius rearrangement to amine hydrochloride **9** and diazotation of **9** with $NaNO_2$ in AcOH to a mixture of **10** and chloride **11**. The latter two products could easily be separated by column chromatography on silica (yields 64% and 16%, respectively). Alternative

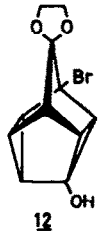



Scheme 1.

routes for the conversion of 7 to 10 were considered viz a Baeyer–Villiger oxidation of 4-homocuneane methylketone and an oxidative decarboxylation with $Pb(OAc)_4/Cu(OAc)_2$ under photolytic conditions†, both were found to be unsuccessful.

Finally, we also examined the Ag(I)-catalyzed isomerization of 1-bromohomocubane-9-one ethylene ketal 4-acetate,[10] which is readily available from homocubane carboxylic acid 4, as a possible route to the homocuneane acetate 10. However, serious problems were encountered in the crucial cage isomerization step.

The homocuneane alcohol 12 could neither be obtained by direct deamination of amine hydrochloride 9 in $H_2O$, nor by LAH reduction of acetate 10 and acid catalyzed transesterification of 10 in ethanol. In all three cases, mixtures of cage opened products were obtained. The free amine of 9 is also very unstable. It should be noted that nortricyclanol is readily accessible from its acetate 1 by LAH reduction.[4a]

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The homoketonization experiments with acetate 10 were performed by treating it with NaOMe in MeOH at room temperature. In a fast reaction, 10 gave a crystalline mixture of two isomeric ketones, m.p. 105–130°, in 86% yield. Separation of these ketones was accomplished by fractional crystallization from $CCl_4$ or careful column chromatography on silica. Structures 13‡ (m.p. 129–131°) and 14‡ (m.p. 155–156°) were assigned on the basis of elemental analysis and spectral data, supported by chemical transformations as will be outlined below (Scheme 2).

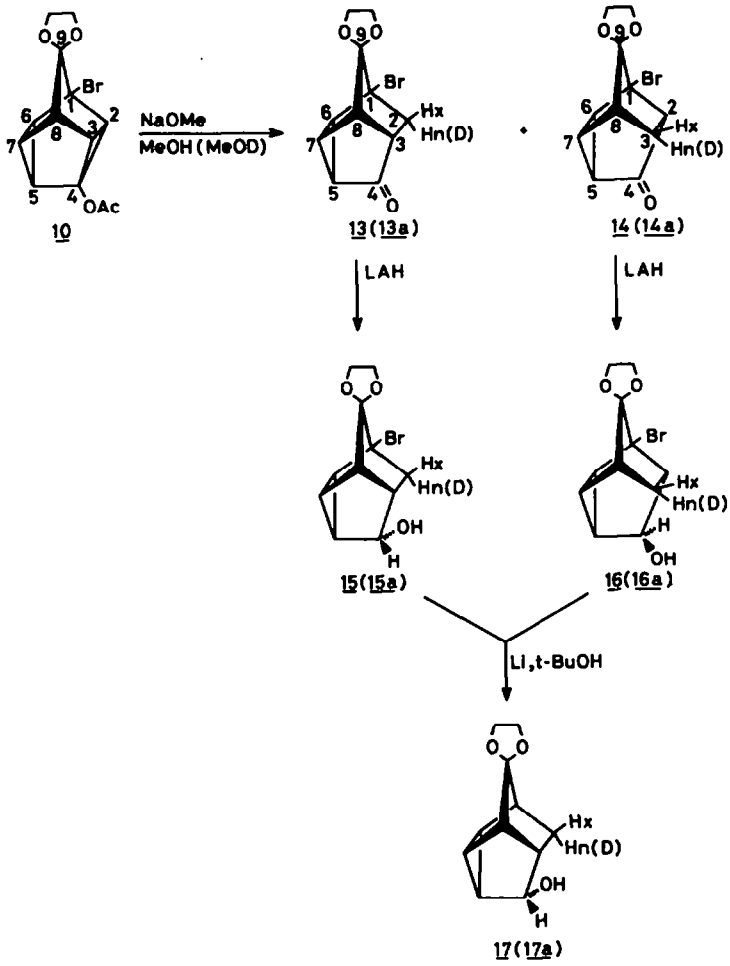
The IR spectra of 13 and 14 exhibited cyclopropane absorptions at 3070 $cm^{-1}$ and typical cyclopentanone absorptions at 1730 and 1725 $cm^{-1}$, respectively. The NMR spectrum of 13 in $CDCl_3$ showed a complicated pattern for the bridgehead protons $H_5$, $H_6$, $H_7$, $H_8$ and the *exo*-proton $H_x$ at $\delta$ 2.22–2.84. An asymmetrical ethylene ketal proton absorption appeared at $\delta$ 3.93–4.42, indicative of the molecular dissymetry in 13.[11] A sharp doublet (one half of an AB pattern) was observed at $\delta$ 1.98 ($J \sim 11$ Hz, geminal coupling with $H_x$) which was attributed to the *endo*-proton $H_n$. This absorption coincided with that of $H_3$. The assignment of $H_n$ is based on the shift reagent experiments (*vide infra*) and the anticipated higher field position of $H_n$ compared with $H_x$, due to either an anisotropic deshielding effect of the ethylene ketal function on $H_x$, a shielding effect of the carbonyl function on $H_n$ or a combination of both effects. Furthermore, molecular models show the dihedral angle for $H_n$, $H_3$ to be very close to 90° which is in accord with $J_{H_n,H_3} \sim 0$ Hz.

Upon the addition of the upfield shift reagent $Pr(fod)_3$ both the doublet and the underlying one proton absorption at $\delta$ 1.98, together with one proton from the complex pattern at $\delta$ 2.22–2.84 showed large upfield shift gradients. These absorptions must be attributed to the protons $H_n$, $H_3$ and $H_5$ resp., as these protons are spatially close to the complexing CO group. Unambiguous assignment of all signals was accomplished with the aid of spin–spin decoupling experiments of the lanthanide complexed compound 13 as shown in Fig. 1.

Irradiation at the doublet assigned to $H_n$ gave the appearance of a new doublet ($J \sim 8$ Hz) at $\delta$ −0.24 attributable to proton $H_x$. Irradiation at this position caused the doublet for $H_n$ at $\delta$ −3.32 to collapse to a singlet. At the same time the triplet at $\delta$ −4.88 changed into a broad singlet revealing the position of $H_3$ ($J_{H_3,H_x} \sim 8$ Hz) and

†Such functional group transformations of a bridgehead COOH to OAc were successful for other strained polycyclic systems. Unpublished observations in the authors lab.

‡For sake of clearness the numbering of the C-atoms is the same as in the starting material. The IUPAC numbering is applied in the Experimental.




Scheme 2.

consequently also the position of $H_5$ ($\delta$ −5.14). On irradiation of $H_3$, *exo*-proton $H_x$ appeared as a doublet ($J_{H_n,H_x} \sim 11$ Hz) at $\delta$ −0.29.

The NMR spectrum of **14** showed a nice doublet ($J_{H_n,H_x} \sim 11$ Hz) for the *endo* proton $H_n$ at $\delta$ 1.54 ppm. In contrast with the spectrum of **13** the expected quartet for the *exo*-proton $H_x$ ($J_{H_x,H_n} \sim 11$ Hz, $J_{H_x,H_3} \sim 8$ Hz) was visible among absorptions of the remaining cage protons. Both $H_n$ and $H_2$ in **14** showed a considerable change in chemical shift as compared with the corresponding protons $H_n$ and $H_3$ in **13**, viz an upfield shift for $H_n$ and a downfield shift for $H_2$ in **14**, which is in full accord with the expected deshielding effect by the adjacent bridgehead bromine atom on these protons in the proposed structures **13** and **14**, respectively. In addition, the use of $Pr(fod)_3$ allowed the observation of a doublet for $H_2$, due to coupling with $H_x$ ($J_{H_2,H_x} \sim 8$ Hz) which can only be reconciled with structure **14**. Under the same conditions, proton $H_3$ in **13** appeared as a broad triplet because of additional splitting by the bridgehead proton $H_8$ ($J_{H_3,H_x} \sim 8$ Hz, $J_{H_3,H_8} \sim 4$ Hz).

The structural relationship between **13** and **14** was unequivocally proven by LAH reduction and subsequent debromination with Li in t-BuOH (Scheme 2). As expected for such half cage ketones, LAH reduction proceeded with a high degree of steric approach control yielding exclusively the oxygen inside alcohols **15** and **16**. In these alcohols the severely congested *endo* proton $H_n$ is strongly deshielded by the OH-function. The spectra of these alcohols were in full agreement with the proposed structures **15** and **16** (Experimental). The bridgehead Br atom at $C_1$ could be easily removed with Li in t-BuOH to give the single alcohol **17**.

The stereochemistry of the cage opening of acetate **10** was studied by performing the homoketonization with NaOMe in MeOD. A mixture of two monodeuterated ketones **13a** and **14a** was obtained. The NMR spectra of both **13a** and **14a** showed the complete absence of the doublets for $H_n$ at $\delta$ 1.98 and $\delta$ 1.54 ppm, respectively. In addition, the $Pr(fod)_3$ shifted PMR spectra showed a doublet ($J \sim 8$ Hz) for the $H_x$ proton in **13a** and a simplified pattern for $H_x$ in **14a** due to the loss of strong geminal coupling. The signals for all other protons remained unchanged. The NMR data clearly indicate the incorporation of the deuterium atom into the *endo* position. Hence, the base catalyzed homoketonization of homocuneane acetate **10** proceeds with exclusive retention of configuration. This result represents the first example of a strained polycyclic molecule containing a cyclopropanol ring which opens with retention of configuration.

In order to exclude any steric and electronic effect of the bromine atom at $C_1$ and of the relatively bulky ethylene ketal function on this stereochemical course, the deketalized and debrominated homocuneane acetates

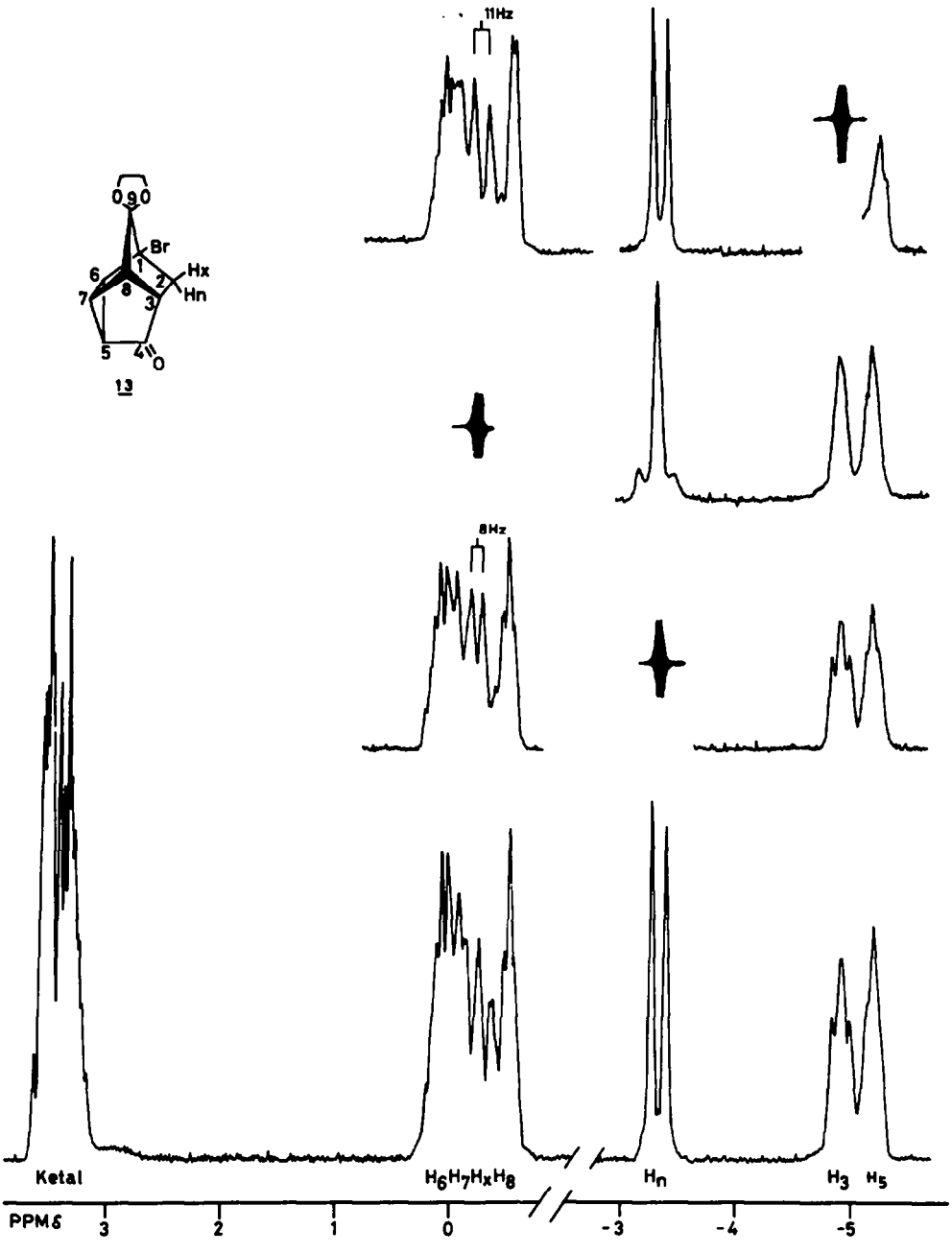


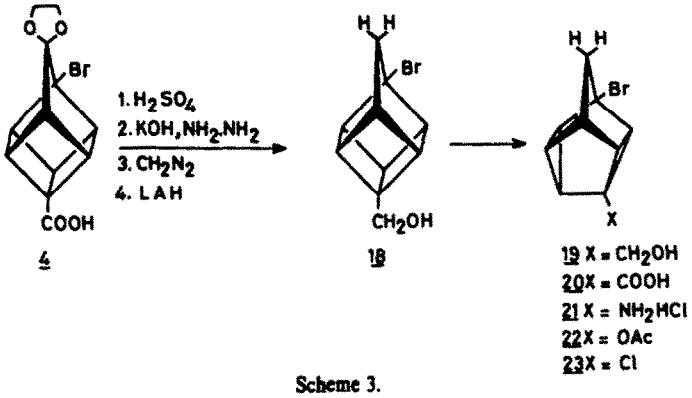

Fig. 1.

22 (Scheme 3) and 31 (Scheme 5) were synthesized, respectively (Experimental for details).

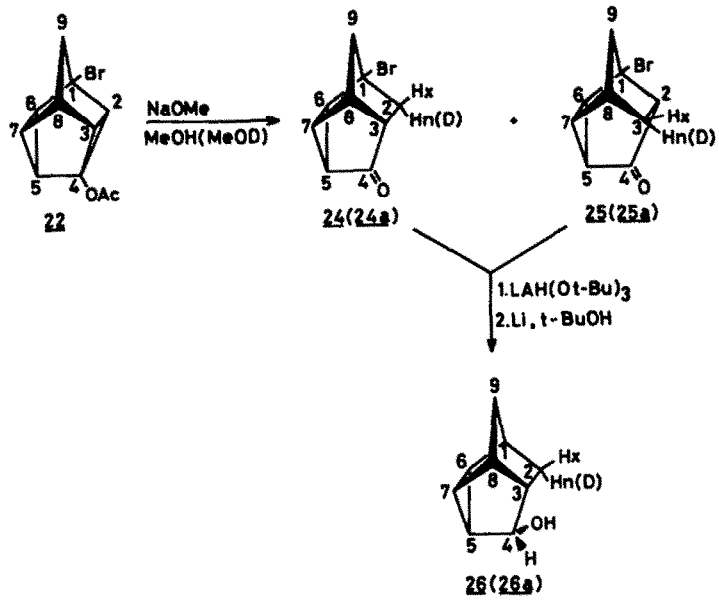
Treatment of acetate 22 with NaOMe in MeOH under the same conditions as described for the ketalized acetate 10, gave a mixture of ketones 24 and 25 in quantitative yield (Scheme 4).

Although several analytical techniques were used, separation of these ketones could not be achieved. The PMR spectrum of the mixture ($CDCl_3$) displayed an extremely complicated pattern between $\delta$ 1.90–3.10 and a sharp doublet for one proton at $\delta$ 1.72 ($J \sim 12$ Hz). When the homoketonization reaction was carried out with NaOMe in MeOD, this doublet together with a one proton absorption in the multiplet was absent in the spectrum of the deuterated ketones. However, the complexity of the spectra did not allow an unambiguous determination of the stereochemistry. To circumvent the separation problem, the mixture of ketones was reduced with $LiAlH(O\text{-}tBu)_3$ and the obtained mixture of alcohols subsequently debrominated with Li in t-BuOH. The single alcohol 26 was isolated in 72% overall yield (Scheme 4). Its structure was unambiguously assigned by IR and NMR fingerprint comparison† with an authentic sample.[12] Detailed unraveling of the spectrum of 26, needed for assigning the signals of $H_n$ and $H_x$, was accomplished by using double resonance techniques on the spectrum of the lanthanide ($Eu(dpm)_3$) complexed compound. As expected large shifts were observed for

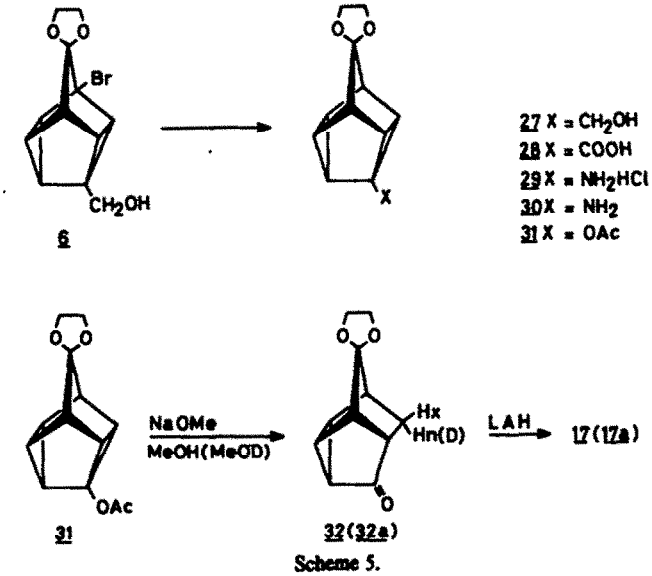
†Prof. A. Nickon kindly provided the spectral data of 26.




Scheme 3.




Scheme 4.




Scheme 5.

protons $H_3$, $H_4$ and *endo*-proton $H_n$. After having established the positions of the crucial protons $H_n$ and $H_x$, the stereochemistry of the ring opening could be readily determined by treating acetate **22** with NaOMe in MeOD and subsequent reduction and debromination of the monodeuterated ketones **24a** and **25a**. NMR analysis of the monodeuterated alcohol **26a** showed that the deuterium incorporation was specifically into the $C_7$-*endo*-position as evidenced by the absence of the $H_n$ proton absorption and the appearance of the *exo*-proton $H_x$ as a doublet ($J_{H_x,H_3} \sim 8$ Hz). Clearly, the stereochemical course of the base induced homoketonization of the deketalized homocuneane acetate **22** is the same as that of the ketal containing substrate **10**. The stereochemistry is not affected by the ketal function.

With NaOMe in MeOH the debrominated acetate **31** was rapidly transformed into ketone **32** (m.p. 73–74°) (Scheme 5). NMR-analysis (Experimental) of both the non-deuterated ketone **32** and mono-deuterated **32a** clearly revealed that the homoketonization proceeds again with exclusive retention of configuration.

The base induced homoketonization of homocuneane acetates is a highly stereospecific process proceeding with exclusive retention of configuration. This stereochemistry is completely opposite to the results, viz. inversion of configuration, obtained by Nickon *et al.*[4] for the cyclopropanol opening in 1-acetoxynortricyclane **1** and 2-acetoxytriaxane **2**, but rather conforms to the general stereochemical pathway observed for the base catalyzed ring opening of cyclobutanol and cyclopentanol containing strained polycyclic structures.[5,6] Conclusively, the stereochemistry of the base induced cyclopropane ring opening in polycyclic molecules is not primarily determined by the specific nature of the cyclopropane ring. The striking difference in stereochemistry of cyclopropanol cleavage in the triaxane and homocuneane system can hardly be attributed to steric factors, as both substrates and their homoketonized products show a strong structural relationship. However, a considerable amount of strain energy is introduced by constructing the homocuneane skeleton from the triaxane system by connecting the $C_6$ and $C_8$ carbon atoms, suggesting that strain effects may play an important role. Additional support for this view was elegantly provided by Miller and Dolce,[13] who recently studied the base catalyzed bis-homoketonization of homocuneane 4,5-diol **33**. They observed exclusive retention of configuration in the first homoketonization step (A) and complete inversion of configuration in the subsequent cyclopropanol ring opening (B) (Scheme 6).

The stereochemical course of the initial cyclopropanol ring opening in homocuneane diol **33** is consistent with our results on the stereospecificity of the ring cleavage of homocuneanes, whereas the inversion of stereochemistry for the subsequent cyclopropanol bond cleavage in the less strained half cage ketone **34** conforms to Nickon's observations on the stereochemistry of the bond cleavage of the triaxane **2**. Although no experimental data on the strain energy of **34** and **2** are available, it is likely that these substrates have about the same energy content.

The remarkable divergency in the stereochemistry of the cyclopropanol ring opening reaction can be explained by considering the effect of strain on the process of bond cleavage of the respective homo-enolate anions. The first step in the homoketonization process involves the formation of a carbanionic species. In highly strained polycyclic structures one may expect that the carbanionic centre will rapidly move away from the developing CO function with a concomitant release of a considerable amount of strain energy. As a consequence, the carbanionic centre will be hardly shielded by the departing CO function and rapidly be protonated on its open face by solvent molecules favorably disposed around the polar CO group. The stereochemical result is retention of configuration.

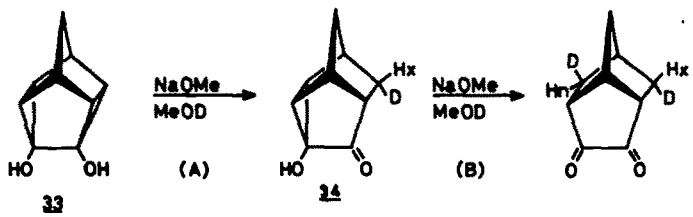
In less strained systems, the strain is not large enough to enforce the carbanionic centre to separate completely from the electrophilic CO function leaving a substantial homoconjugative stabilization of the incipient carbanionic species. Protonation of this carbanionic species in which the *endo*-side is homoconjugatively shielded by the carbonyl group, will preferentially take place from the *exo*-side and accordingly will result in inversion of configuration.

In conclusion, we suggest that the stereochemical course of the base induced homoketonization of strained polycyclic alcohols, in general, is highly dependent on the possibility for homoconjugative stabilization during the C–C bond cleavage of the homoenolate anion. Effective homoconjugative stabilization can only be envisaged in those cases where the strain energy associated with the C–C bond to be cleaved in the homoketonization process permits effective orbital overlap.

In acid media the cleavage of cyclopropanols generally occurs with retention of configuration at the site of electrophilic attack.[3b,4a] The homoenols and homoenolacetates which have been studied include 1-acetoxynortricyclane **1** and 2-acetoxytriaxane **2**. Until recently, this stereochemical pathway was accepted as a general characteristic for the $SE_2$ reaction. However, Nickon *et al.*[4b,14] demonstrated that both steric factors and solvent combinations can play a dramatic role in controlling the stereochemistry of this ring opening in polycyclic structures. As shown above, strain features in the polycyclic systems may also be of importance in determining the stereochemistry of the acid induced homoketonization. Therefore, we investigated the acid catalyzed cyclopropanol ring opening in the homocuneane system.

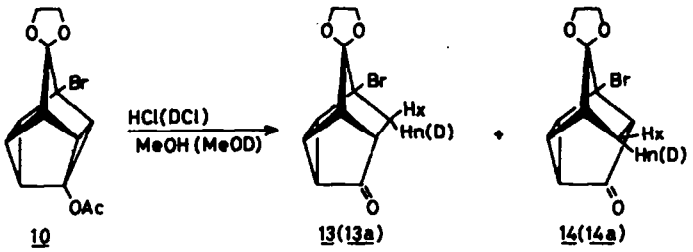
Treatment of acetate **10** with HCl (aq) in MeOH at room temperature afforded a mixture of ring opened ketones **13** and **14** (Scheme 7).

The stereochemistry of this $SE_2$ reaction was established by performing the reaction in $DCl/CH_3OD$. A




33 34

Scheme 6.




10 13(13a) 14(14a)

Scheme 7.

mixture of mono-deuterated ketones **13a** and **14a** was obtained. NMR-analysis unequivocally showed that deuterium was introduced exclusively at the *endo*-positions. Evidently, the acid catalyzed homoketonization of homocuneane acetate **10** takes place with retention of configuration. This result nicely conforms to the general pattern of the $SE_2$ type reaction in cyclopropanols.

## EXPERIMENTAL

IR spectra were taken on a Perkin–Elmer 257 grating spectrometer. NMR spectra were recorded on a Varian HA-100, Varian EM-390 or Bruker WH-90, using TMS as internal standard. Mass spectra were recorded on a Varian SM-1B spectrometer. All m.ps are uncorrected. Elemental analyses were carried out in the micro analytical department of the University of Groningen under supervision of Mr. D. Hamminga, and in the micro analytical department of the University of Nijmegen under supervision of Mr. J. Diersmann.

1-*Bromopentacyclo*[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*nonan-9-one ethylene ketal 4-carboxylic acid* (**4**) was prepared in 70–80% yield as described by Key,[8,15] m.p. 187–189°.

4-(1-*Bromopentacyclo*[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*nonyl-9-one ethylene ketal*)*carbinol* (**5**) was prepared in quantitative yield as described by Key,[15] m.p. 84–87°.

4-(1-*Bromopentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonyl-9-one ethylene ketal*)*carbinol* (**6**). $AgNO_3$ (1.0 g, 5.9 mmole) was added to a soln of **5** (1.0 g, 3.5 mmole) in MeOH (20 ml) and $H_2O$ (5 ml). After refluxing for 24 hr, the MeOH was evaporated, the residue diluted with water and extracted with $CHCl_3$. The combined $CHCl_3$ layers were washed with NaCl aq (sat) and water, and subsequently dried ($MgSO_4$). Solvent was removed yielding alcohol **6** as a yellow oil which crystallized after addition of a little ether (0.8 g, 80%). Recrystallization from n-hexane gave a pure sample, m.p. 101–103°; IR $\nu_{max}^{KBr}$ 3360, 3260 (O–H), 3050 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.86–4.38 (m, 4H, ketal group), 3.78 (AB q, J ~ 12 Hz, 2H, $-CH_2-O-$), 1.90–2.48 (m, 6H), 1.92 (s, 1H, OH); *m/e* 284, 286 ($M^+$, 1Br). (Found: C, 50.92; H, 4.64; Br, 28.11. Calc. for $C_{12}H_{13}BrO_3$: C, 50.55; H, 4.60; Br, 28.03%).

1 - *Bromopentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonan* - 9 - *one ethylene ketal 4-carboxylic acid* (**7**). Benzene (30 ml), tetrabutylammoniumbromide (0.5 g, 1.6 mmole) and **6** (3.2 g, 11.2 mmole) were added to a soln of $KMnO_4$ (4.8 g, 30.4 mmole) in water (50 ml).[9] After stirring at room temp. for 3 days, 5% $NaHSO_3$ aq was added to destroy the excess of $KMnO_4$. The $MnO_2$ ppt was filtered off, the water layer separated and acidified with 6% HCl aq. The crude acid **7** was filtered off, washed with water and dried *in vacuo* ($CaCl_2$) (2.63 g, 78%). Crystallization from acetone gave an analytically pure sample, decomposition >260°. IR $\nu_{max}^{KBr}$ 1675 (C=O) $cm^{-1}$, NMR ($D_2O$–NaOH, $\delta$ 4.30–4.70 (m, 4H, ketal group), 2.32–2.30 (m, 6H); *m/e* 298, 300 ($M^+$, 1Br). (Found: C, 48.21; H, 3.67; Br, 26.59; Calc. for $C_{12}H_{11}BrO_4$: C, 48.16; H, 3.68; Br, 26.76%).

1 - *Bromopentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonan* - 9 - *one ethylene ketal 4-amino hydrochloride* (**9**). To a stirred ice-cooled soln of **7** (14.0 g, 0.047 mole) in acetone (100 ml) and water (4 ml) was added dropwise $Et_3N$ (4.8 g, 0.047 mole) in acetone (100 ml). After addition, a soln of ethyl chloroformate (6.6 g, 0.061 mole) in acetone (22 ml) was added during 45 min, then the mixture stirred for 30 min at 0° and a soln of $NaN_3$ (4.6 g, 0.071 mole) in water (16 ml) added. After being stirred fro 2 hr at 0°, the mixture was poured onto crushed ice and extracted with benzene. The benzene layer was dried ($MgSO_4$) and evaporated to give **8** as a crystalline solid; IR bands at 2140 ($N_3$) and 1700 (C=O) $cm^{-1}$. The azide was dissolved in anhyd benzene and refluxed for 6 hr. Solvent was removed *in vacuo* affording the isocyanate as an oil, which crystallized on standing. IR $\nu_{N=C=O}$ 2270 $cm^{-1}$. The crude isocyanate was dissolved in THF (100 ml), conc HCl (24 ml) was added and the mixture heated under reflux for 2 hr. The THF was removed *in vacuo*, the residue diluted with distilled water and ether extracted. The aqueous layer was evaporated to dryness giving the crude amine hydrochloride **9** (11.0 g, 76%), m.p. 194–197°. IR $\nu_{max}^{KBr}$ 3100–2500, 2000, 1600 and 1510 $cm^{-1}$; NMR ($D_2O$) $\delta$ 4.28–4.66 (m, 4H, ketal group), 2.44–3.20 (m, 6H); *m/e* 269, 271 ($M^+$–HCl, 1Br).

1 - *Bromopentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonan* - 9 - *one ethylene ketal 4-acetate* (**10**). $NaNO_2$ (16.0 g, 0.232 mole) was added in small portions during 2 hr to a soln of **9** (4.0 g, 0.013 mole) in AcOH (80 ml). After stirring at room temp. for 20 hr, the soln was neutralized with 5% $NaHCO_3$ aq. The mixture was chloroform extracted and the organic phase washed with 5% $NaHCO_3$ aq and water. After drying ($MgSO_4$), solvent was removed yielding a yellow oil (3.24 g). GLC (column: SE 30, 1/8 in temp. 200°) showed the presence of 2 components. The oil was dissolved in toluene and chromatographed over silica. Elution with toluene furnished the 1 - bromo - 4 - chloropentacyclo-[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonan - 9 - one ethylene ketal **11** (0.6 g, 16%). Recrystallization from EtOH gave a pure sample, m.p. 105–106°. IR $\nu_{max}^{KBr}$ 3070 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.80–4.30 (m, 4H, ketal group). 1.96–2.60 (m, 6H); *m/e* 290 ($M^+$, 1Br, 1Cl). (Found: C, 45.94; H, 3.42; Cl, 12.30; Br, 27.68. Calc. for $C_{11}H_{10}BrClO_2$: C, 45.62; H, 3.48; Cl, 12.25; Br, 27.59%). Further elution with $CHCl_3$ yielded **10** (2.63 g, 64%). Recrystallization from $CHCl_3$/pet. ether 60–80° gave an analytically pure sample, m.p. 81–84°. IR $\nu_{max}^{KBr}$ 3065 (cyclopropyl H), 1750 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.84–4.30 (m, 4H, ketal group), 1.96–2.60 (m, 6H), 2.02 (s, 3H, $-O-\overset{O}{\overset{\|}{C}}-CH_3$); *m/e* 312, 314 ($M^+$, 1Br). (Found: C, 50.05; H, 4.20; Br, 25.89. Calc. for $C_{13}H_{13}BrO_4$: C, 49.87; H, 4.19; Br, 25.52%).

*Ring opening of acetate* **10** *with* NaOMe *in* MeOH. NaOMe (0.5 g, 9.2 mmole) was added to a stirred soln of **10** (1.0 g, 3.2 mmole) in MeOH (25 ml). After stirring at room temp. for 1 hr, water was added and the mixture extracted with ether. The ether layer was dried ($MgSO_4$) and the solvent evaporated to give a mixture of **13** and **14** (0.75 g, 86%) as a crystalline solid. The solid was dissolved in toluene and chromatographed over silica (Merck, H Nach Stahl, typ 60). Elution with toluene/chloroform (1:5) successively gave **14**, a mixture of **13** and **14** and ketone **13**. Recrystallization from $CCl_4$ (3x) gave pure samples. 8-*Bromotetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan-5,9-dione 9-ethylene ketal* **13**, m.p. 129–131°; IR $\nu_{max}^{KBr}$ 3070, 3035 (cyclopropyl H), 1730 (C=O) $cm^{-1}$; NMR ($C_6D_6$) $\delta$ 3.20–4.00 (m, 4H, ketal group), 2.20–2.80 (m, 1H, $H_x$), 1.43–2.33 (m, 5H), 1.78 (d, $J_{a,x}$ ~ 11 Hz, 1H, $H_a$); NMR ($CDCl_3$) $\delta$ 3.93–4.42 (m, 4H, ketal group), 2.55–2.84 (m, 2H, $H_x$ and $H_1$), 2.22–2.55 (m, 3H, $H_{2,3,4}$), 1.85–2.15 (2H, m for $H_4$, d for $H_a$ at 1.98, $J_{a,x}$ ~ 11 Hz); *m/e* 270, 272 ($M^+$, 1Br). (Found: C, 48.38; H, 4.06; Br, 29.63. Calc. for $C_{11}H_{11}BrO_2$: C, 48.73; H, 4.09; Br, 29.48%). 1-*Bromotetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonane-5,9-dione* 9-

*ethylene ketal* **14**, m.p. 155–156°; IR $\nu_{max}^{KBr}$ 3080, 3070 (cyclopropyl H), 1725 (C=O) $cm^{-1}$; NMR ($C_6D_6$) $\delta$ 3.20–4.00 (m, 4H, ketal group), 2.47–2.87 (m, 2H, $H_6$ and $H_8$), 1.90–2.47 (m, 1H, $H_x$), 1.30–1.90 (m, $H_{2,3,4}$), 1.20 (d, $J_{a,x} \sim 11$ Hz, 1H, $H_a$); NMR ($CDCl_3$) $\delta$ 3.89–4.44 (m, 4H, ketal group), 2.77–3.00 (m, 1H, $H_8$), 2.29–2.70 (m, 2H, $H_x$ and $H_6$), 2.04–2.24 (m, 3H, $H_{2,3,4}$), 1.54 (d, $J_{a,x} \sim 11$ Hz, 1H, $H_a$); *m/e* 270, 272 ($M^+$, 1 Br). (Found: C, 48.53; H, 4.05; Br, 29.68. Calc. for $C_{11}H_{11}BrO_3$: C, 48.73; H, 4.09; Br, 29.48%). In an original mixture the ratio of **13** and **14** (4:1) could be determined by the integral ratio of the signals at $\delta$ 1.98 ($H_a$ of **13**) and $\delta$ 1.54 ($H_a$ of **14**).

**8** - *Bromo* - 7 - endo - *deuteriotetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan*-5,9 - *dione* **9**-*ethylene ketal* (**13a**) *and* **1** - *bromo* - 7 - *endo-deuteriotetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan*-5,9-*dione* **9** *ethylene ketal* (**14a**) were prepared as described above using MeOD instead of MeOH; Ketone **13a**, m.p. 130.5–132°; IR $\nu_{max}^{KBr}$ 3070, 3030 (cyclopropyl H), 1725 (C=O) $cm^{-1}$; NMR ($C_6D_6$) $\delta$ 3.20–4.00 (m, 4H, ketal group), 2.52 (d, $J_{Hx,H6} \sim 8$ Hz, 1H, $H_x$), 1.70–2.30 (m, 4H), 1.30–1.70 (m, 1H, $H_6$); NMR ($CDCl_3$) $\delta$ 3.93–4.44 (m, 4H, ketal group), 2.48–2.84 (m, 2H, $H_x$ and $H_1$), 2.26–2.48 (m, 3H, $H_{2,3,4}$), 1.91–2.15 (m, 1H, $H_6$); *m/e* 271, 273 ($M^+$, 1 Br). (Found: C, 48.73; H, 3.75; Br, 29.80; Calc. for $C_{11}H_{10}DBrO_3$ C, 48.55; H, 3.70; Br, 29.37%). Ketone **14a**, m.p. 155–157°; NMR ($CDCl_3$) $\delta$ 3.83–4.47 (m, 4H, ketal group), 2.60–3.00 (m, 1H, $H_8$), 2.30–2.60 (m, 2H, $H_x$ and $H_6$), 1.93–2.23 (m, 3H, $H_{2,3,4}$); *m/e* 271, 273 ($M^+$, 1 Br).

**8** - *Bromo* - 5 - endo - *hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan* - 9 - *one ethylene ketal* (**15**). A soln of **13** (1.0 g, 3.7 mmole) in anhyd ether (25 ml) was added to a suspension of LAH (0.3 g, 7.9 mmole) in anhyd ether (25 ml). After refluxing for 3 hr, the mixture was diluted with water and ether extracted. The ether layer was dried ($MgSO_4$) and concentrated to give **15** (0.9 g, 98%). Recrystallization from $CHCl_3$/pet-ether 60–80° gave an analytically pure sample, m.p. 93–94°; IR $\nu_{max}^{KBr}$ 3300 (OH), 3060 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.44 (m, 1H, $H_5$), 3.80–4.34 (m, 4H, ketal group), 3.18 (broad s, 1H, OH), 1.52–2.40 (m, 7H); *m/e* 272, 274 ($M^+$, 1 Br). (Found: C, 48.09; H, 4.84. Calc. for $C_{11}H_{13}BrO_3$: C, 48.38; H, 4.80%).

**8** - *Bromo* - 7 - endo - *deuterio* - 5 - endo - *hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan* - 9 - *one ethylene ketal* (**15a**) was prepared as described above using monodeuterated ketone **13a** as the starting material. Recrystallization from $CHCl_3$/pet-ether 60–80° gave an analytically pure sample, m.p. 92–94°; IR $\nu_{max}^{KBr}$ 3300 (OH), 3060 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.46 (broad s, 1H, $H_5$), 3.82–3.34 (m, 4H, ketal group), 2.74 (d, $J_{H5,OH} \sim 3$ Hz, 1H, OH), 1.52–2.32 (m, 6H); *m/e* 273, 275 ($M^+$, 1 Br).

**1** - *Bromo* - 5 - endo - *hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan* - 9 - *one ethylene ketal* (**16**). The same procedure as for the preparation of alcohol **15** was used. A 90% yield of **16** was obtained from **14**. Recrystallization from $CHCl_3$/pet-ether 60–80° and subsequent sublimation (5 mm/80°) afforded an analytically pure sample, m.p. 99–100°; IR $\nu_{max}^{KBr}$ 3250 (OH), 3050 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.70 (d, $J_{H5,H6} \sim 6$ Hz, 1H, $H_5$), 3.78–4.30 (m, 4H, ketal group), 2.78 (broad s, 1H, OH), 1.26–2.40 (m, 7H); *m/e* 272, 274 ($M^+$, 1 Br). (Found: C, 48.21; H, 4.85; Br, 29.60; Calc. for $C_{11}H_{13}BrO_3$: C, 48.38; H, 4.80; Br, 29.26%).

5-Endo-*hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan*-9-*one ethylene ketal* (**17**). Finely cut pieces of Li (0.144 g, 20.9 mmole) were gradually added to a stirred mixture of **15** (0.944 g, 3.46 mmole), t-BuOH (0.615 g, 8.3 mmole) and anhyd THF (25 ml) under $N_2$. After refluxing for 30 hr, water was added dropwise to destroy the excess of Li, the mixture chloroform extracted and dried ($MgSO_4$). Solvent was removed, yielding **17** as a crystalline solid (0.62 g, 92%). Recrystallization from $CHCl_3$/pet-ether 60–80° (2x) gave an analytically pure sample, m.p. 99–101°; IR $\nu_{max}^{KBr}$ 3280 (OH), 3080, 3060, 3030 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.44 (broad s, 1H, $H_5$), 3.82 (s, 4H, ketal group), 2.22 (broad s, 1H, OH), 1.18–2.16 (m, 7H), 1.66 (d, $J_{Ha,Hx} \sim 11$ Hz, 1H, $H_a$); *m/e* 194 ($M^+$). (Found: C, 67.72; H, 7.18; Calc. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27%). This alcohol **17** was also obtained using the same procedure, starting from alcohol **16**.

**7** - Endo - *deuterio* - 5 - endo - *hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonal* - 9 - *one ethylene ketal* (**17a**) was prepared as described above using monodeuterated alcohol **15a** as the starting material. Recrystallization from $CHCl_3$/pet-ether 60–80° gave an analytically pure sample, m.p. 98.5–101°; IR $\nu_{max}^{KBr}$ 3420 (OH), 3050 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.56 (broad s, 1H, $H_5$), 3.97 (s, 4H, ketal group), 2.86 (s, 1H, OH), 1.26–2.44 (m, 7H); *m/e* 195 ($M^+$).

**4** - (**1** - *Bromopentacyclo*[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*nonyl*)*carbinol* (**18**) was prepared as described by Klunder and Zwanenburg,[16] m.p. 44–46°.

**4**-(**1**-*Bromopentacyclo*[4,3,0,$0^{2,4}$,$0^{3,8}$,$0^{5,7}$]*nonyl*)*carbinol* (**19**). The same procedure as for the preparation of **6** was used. After refluxing for 10 hr homocubane carbinol **18** gave **19** as a yellow oil which was purified over silica ($CHCl_3$–ether 1:1) (93%). Recrystallization from pentane gave an analytically pure sample, m.p. 71–72°; IR $\nu_{max}^{KBr}$ 3230, 3140, 3050, 3020 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.80 (AB q, $J \sim 12$ Hz, 2H, $-CH_2O-$), 2.10–2.80 (m, 9H); *m/e* 226, 228 ($M^+$, 1 Br). (Found: C, 53.09; H, 4.86; Br, 35.01; Calc. for $C_{10}H_{11}BrO$: C, 52.89; H, 4.88; Br, 35.19%).

**1**-*Bromopentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonane* **4**-*carboxylic acid* (**20**). The same procedure as for the oxidation of **6** was used. After stirring at room temp. for 20 hr, **19** yielded **20** in 74%, m.p. 174–177° (acetone); IR $\nu_{max}^{KBr}$ 1680 (C=O) $cm^{-1}$; NMR ($CD_3OD$) $\delta$ 2.20–3.10 (m, 8H); *m/e* 240, 242 ($M^+$, 1 Br). (Found: C, 49.90; H, 3.68; Br, 33.02; Calc. for $C_{10}H_9BrO_2$: C, 49.82; H, 3.76; Br, 33.15%).

**1**-*Bromopentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonane* **4**-*amino hydrochloride* (**21**). The same procedure as for the preparation of amine hydrochloride **9** was used. A 91% yield of crude amine hydrochloride **21** was obtained from **20**. IR $\nu_{max}^{KBr}$ 3380, 3200–2300, 1550 and 1500 $cm^{-1}$; NMR ($CD_3OD$) $\delta$ 2.30–2.90 (m, 8H); *m/e* 211, 213 ($M^+$–HCl, 1 Br). This crude amine hydrochloride was used for the preparation of acetate **22**.

**1**-*Bromopentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonane* **4**-*acetate* (**22**). The same procedure as for the preparation of **10** was used. Starting from **21**, a mixture of chloride **23** and acetate **22** was obtained which could be separated by column chromatography on silica. Elution with pentane afforded **1**-*bromo*-**4**-*chloropentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonane* **23** as a colourless oil (11%). IR $\nu$ 3050 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 2.10–2.84 (m, 8H); *m/e* 232 ($M^+$, 1 Br, 1 Cl). Further elution with toluene gave **22** as a colourless oil (44%) IR $\nu$ 3050 (cyclopropyl H), 1750, sh at 1765 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 2.18–2.84 (m, 8 H), 2.06 (s, 3 H, $-O-\overset{O}{\overset{\|}{C}}-CH_3$); *m/e* 254, 256 ($M^+$, 1 Br).

5-Endo-*hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonane* **26**. NaOMe (285 mg, 5.3 mmole) was added to a stirred soln of **22** (460 mg, 1.8 mmole) in MeOH (25 ml). After stirring at room temp. for 5 min, water was added and the mixture extracted with ether. The ether layer was dried ($MgSO_4$) and the solvent evaporated to give a mixture of **24** and **25** as a colourless oil (100%) which solidified on treatment with hot pentane (3x), m.p. 61–65°. IR $\nu_{max}^{KBr}$ 3060 (cyclopropyl H), 1730 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.90–3.10 (complex pattern), 1.72 (d, $J \sim 12$ Hz, 1 H); *m/e* 212, 214 ($M^+$, 1 Br). A soln of **24** and **25** (274 mg, 1.3 mmole) in anhyd THF (15 ml) was added to a suspension of LAH (Ot-Bu)$_3$ (350 mg, 1.4 mmole) in anhyd THF (10 ml). After stirring at room temp. for 5 hr, water was added and the mixture extracted with ether. The ether layer was dried ($MgSO_4$) and concentrated to give the alcohols **8**-*bromo*-5-endo-*hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonane* (**A**) and **1**-*bromo*-5-endo-*hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonane* (**B**) as a colourless oil (251 mg, 90%). IR $\nu$ 3340 (OH), 3030 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.88 (d of m, $J_{H5,H6} \sim 5.5$ Hz, 1 H, $H_5$ of **B**), 4.60 (d of d, $J_1$ ($H_5$, $H_4$) $\sim 5.5$ Hz, $J_2 \sim 2$ Hz, 1 H, $H_5$ of **A**) 3.40 (s, 1 H, OH), 1.44–2.62 (complex pattern). On basis of the integral ratio of the signals at $\delta$ 4.88 ($H_5$ of **B**) and $\delta$ 4.60 ($H_5$ of **A**) the ratio of **B** and **A** was determined to be 1:4. Finely cut pieces of Li (77 mg, 11.2 mmole) were added to a stirred mixture of alcohols **A** and **B** (236 mg, 1.1 mmole), t-BuOH (162.8 mg, 2.2 mmole) and anhyd THF (10 ml) under $N_2$. After refluxing for 4 days the debromination was almost complete. Water was added dropwise to destroy the excess of Li, the mixture was ether extracted and dried ($MgSO_4$). Solvent was removed, yielding a semi solid. Repeated sublimation gave almost pure **26**, (120 mg, 80%). An

analytically pure sample of **26** could be obtained by preparative GLC (6 ft 10% SE 30 chrom W 60–80), m.p. 142–144° (sealed tube) (lit.[14] 143.5–145.5°); IR $\nu$ ($CCl_4$) 3620 (OH), 3030 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.55 (d, $J_{H_3,H_4} \sim 6$ Hz, 1 H, $H_3$), 2.19 (s, 1 H, OH), 1.28–2.46 (m, 9 H), 0.95 (m, 1 H, $H_x$); *m/e* 136 ($M^+$).

7 - Endo - *deuterio* - 5 - endo - *hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonane* (**26a**) was prepared as described above using MeOD instead of MeOH for the homoketonization of **22**, m.p. 142–145° (sealed tube); IR $\nu$ 3320 (OH), 3030 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 4.55 (d, $J_{H_3,H_4} \sim 6$ Hz, 1 H, $H_3$), 1.18–2.64 (m, 8 H + OH), 0.93 (d, $J_{H_x,H_4} \sim 8$ Hz, 1 H, $H_x$); *m/e* 137 ($M^+$).

4 - (*Pentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonyl* - 9 - *one ethylene ketal*)-*carbinol* (**27**). Finely cut pieces of Li (1.2 g, 173.9 mmole) were gradually added to a stirred mixture of **6** (4.2 g, 14.7 mmole), t–BuOH (4.7 g, 63.5 mmole) and anhyd THF (50 ml) under $N_2$. After refluxing for 14 hr, water was added dropwise, the mixture stirred for another hr, extracted with chloroform and treated with charcoal. After drying ($MgSO_4$) solvent was removed yielding **27** as a yellow oil (2.3 g, 76%). Chromatography over silica ($CHCl_3$) gave a pure sample. IR $\nu$ 3400 (OH), 3040 (cyclo propyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.93 (s, 4H, ketal group), 3.80 (s, 2H, $-CH_2-O-$) 2.38 (m, 2H), 1.93–2.24 (m, 5H), 1.69 (broad s, 1H, OH); *m/e* 206 ($M^+$).

*Pentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonan-9-one ethylene ketal* 4-*carboxylic acid* (**28**). The same procedure as for the oxidation of **6** was used. The water layer was carefully neutralized with HCl aq (6%). The white ppt was filtered off, washed with water and dried *in vacuo* ($CaCl_2$) (1.4 g, 65%). The filtrate was continuously extracted with ether for 3 days. After drying ($MgSO_4$) solvent was removed yielding a second crop of **28** (0.2 g, 9%). Crystallization from acetone gave an analytically pure sample, decomposition >210° (sealed tube); IR $\nu_{max}^{KBr}$ 1670 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 10.71 (broad s, 1 H, OH), 3.93 (s, 4 H, ketal group), 2.76 (m, 2 H), 2.40–2.62 (m, 3 H), 1.98–2.18 (m, 2 H); *m/e* 220 ($M^+$). (Found: C, 65.01; H, 6.19 Calc. for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49%). Considerable deketalization of **28** took place on acidification of the water layer with HCl aq (6%) affording pentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonan-9-one 4-carboxylic acid, decomposition >215°; IR $\nu_{max}^{KBr}$ 1760, 1670 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 11.0 (broad s, 1 H, OH), 2.60–2.93 (m, 5 H), 2.18 (m, 2 H); *m/e* 176 ($M^+$). (Found: C, 67.61; H, 4.82. Calc. for $C_{10}H_8O_3$: C, 68.18; H, 4.58%).

*Pentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonan-9-one ethylene ketal* 4-*amino hydrochloride* (**29**). The same procedure as for the preparation of **9** was used. Acid **28** gave the amine hydrochloride **29** in 52% yield, m.p. 144–154°; IR $\nu_{max}^{KBr}$ 3420, 3200–2400 $cm^{-1}$. The crude **29** was dissolved in water, treated with 5% $NaHCO_3$ aq and chloroform extracted (2x). The organic phase was washed with 5% $NaHCO_3$ aq and water, and subsequently dried ($MgSO_4$). Solvent was removed yielding **30** as a colourless oil which slowly decomposed on standing at room temp. IR $\nu$ 3350 ($NH_2$), 3030 (cyclopropyl H) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.83 (s, 4 H, ketal group), 1.87–2.53 (m, 9 H). This amine was pure enough for further transformations.

*Pentacyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]*nonan-9-one ethylene ketal* 4-*acetate* (**31**). $NaNO_2$ (3.0 g, 43.5 mmole) was added in small portions during 1 hr to a soln of **30** (0.5 g, 2.6 mmole) in AcOH (20 ml). After stirring at room temp. for 24 hr the soln was neutralized with 5% $NaHCO_3$ aq. The mixture was ether extracted and the ether phase washed with 5% $NaHCO_3$ aq and water, and subsequently dried ($MgSO_4$). After treatment with charcoal solvent was removed yielding **31** as a colourless oil, which solidified on standing (0.2 g, 32%). Recrystallization from hexane gave a pure sample, m.p. 72.5–73°; IR $\nu_{max}^{KBr}$ 3060 (cyclopropyl H), 1745 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.80 (s, 4 H, ketal group), 2.16–2.46 (m, 5 H), 1.90–2.16 (m, 2 H), 1.98 (s, 3 H, $-O-\overset{O}{\overset{\|}{C}}-CH_3$); *m/e* 234 ($M^+$).

*Tetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan-5,9-dione* 9-*ethylene ketal* (**32**) NaOMe (0.24 g, 4.4 mmole) was added to a stirred soln of **31** (0.36 g, 1.5 mmole) in MeOH (25 ml). After stirring at room temp. for 1 hr, water was added and the mixture extracted with ether (2x). The organic phase was washed with water, dried ($MgSO_4$) and the solvent evaporated to give **32** as a yellow oil which crystallized on standing (0.18 g, 61%). Recrystallization from $CCl_4$/pet-ether 60–80° gave a pure sample, m.p. 73–74°; IR $\nu$ 3050 (cyclopropyl H), 1720 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.86 (m, 4 H, ketal group), 1.74–2.64 (m, 7 H), 1.46 (d, $J_{H_a,H_x} \sim 10$ Hz, 1 H, $H_a$); *m/e* 192 ($M^+$).

7 - Endo - *deuteriotetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan* - 5,9 - *dione* 9-*ethylene ketal* (**32a**) was prepared as described above using MeOD instead of MeOH. Purification by prep. TLC (0.5 mm $SiO_2$, toluene/MeOH 8:1) gave a pure sample, m.p. 71–72°; IR $\nu$ ($CCl_4$) 3050 (cyclopropyl H), 1730 (C=O) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.96 (m, 4 H, ketal group), 1.86–2.74 (m, 7 H); *m/e* 193 ($M^+$).

5 - Endo - *hydroxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan* - 9 - *one* 9-*ethylene ketal* (**17**). A soln of **32** (126 mg, 0.7 mmole) in anhyd ether (25 ml) was added to a suspension of LAH (100 mg, 2.6 mmole) in anhyd ether (15 ml). After stirring for 30 min at room temp. the mixture was diluted with water and ether extracted. The ether layer was dried ($MgSO_4$) and concentrated to give **17** (80%). Recrystallization from $CHCl_3$/pet-ether 60–80° gave a pure sample, m.p. 99–101°; Spectral and physical data are identical with those obtained from **17**, prepared by homoketonization of **10** followed by reduction of **13** and debromination of **15**.

7 - Endo - *deuterio* - 5 - endo - *hydroxytetracyclo* - [4.3.0.$0^{2,4}$.$0^{3,8}$]*nonan* - 9 - *one* 9-*ethylene ketal* (**17a**) was prepared as described above using monodeuterated ketone **32a** as the starting material. Spectral and physical data are identical with those obtained from **17a** prepared by homoketonization of **10** in MeOD followed by reduction of **13a** and debromination of **15a**.

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