Tetrahedron. Vol. 29, pp. 1683 to 1689. Pergamon Press 1973. Printed in Great Britain

CHEMISTRY OF STRAINED POLYCYCLIC COMPOUNDS–VI[1,2]

STEREOSPECIFIC BASE INDUCED HOMOKETONIZATION OF CUBANE, HOMOCUBANE AND 1,3-BISHOMOCUBANE BRIDGEHEAD ALCOHOLS

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(*Received in the UK* 28 *October* 1972; *Accepted for publication* 9 *January* 1973)

Abstract—The base induced homoketonization of bridgehead cubane alcohol **10**, homocubane alcohol **1** and acetate **7**, and 1,3-bishomocubane alcohols **13** and **17** has been studied. Under protic conditions, homocubane alcohol **1** and acetate **7** are converted quantitatively into half cage ketones **3** and **8**, respectively, by exclusive cleavage of the C_4—C_7 bond. Similarly, homoketonization of 1,3-bishomocubane alcohols **13** and **17** leads to half cage ketones **15** and **18**, respectively, by exclusive cleavage of the C_2—C_5 bond. As shown by deuterium labeling experiments homoketonization of **1**, **7**, **13** and **17** proceeds with high stereospecificity and with retention of configuration (> 96%) at the carbon of substitution. The cubane alcohol **10** gave, under similar conditions, complex mixtures of ring-opened products. Under aprotic conditions, base treatment of homocubane alcohol 1 leads to cleavage of the C_3—C_4 and C_2—C_5 bond giving the tricyclo[4.2.1.0.^{2,5}]nonene 21. The mechanism of homoketonization is discussed.

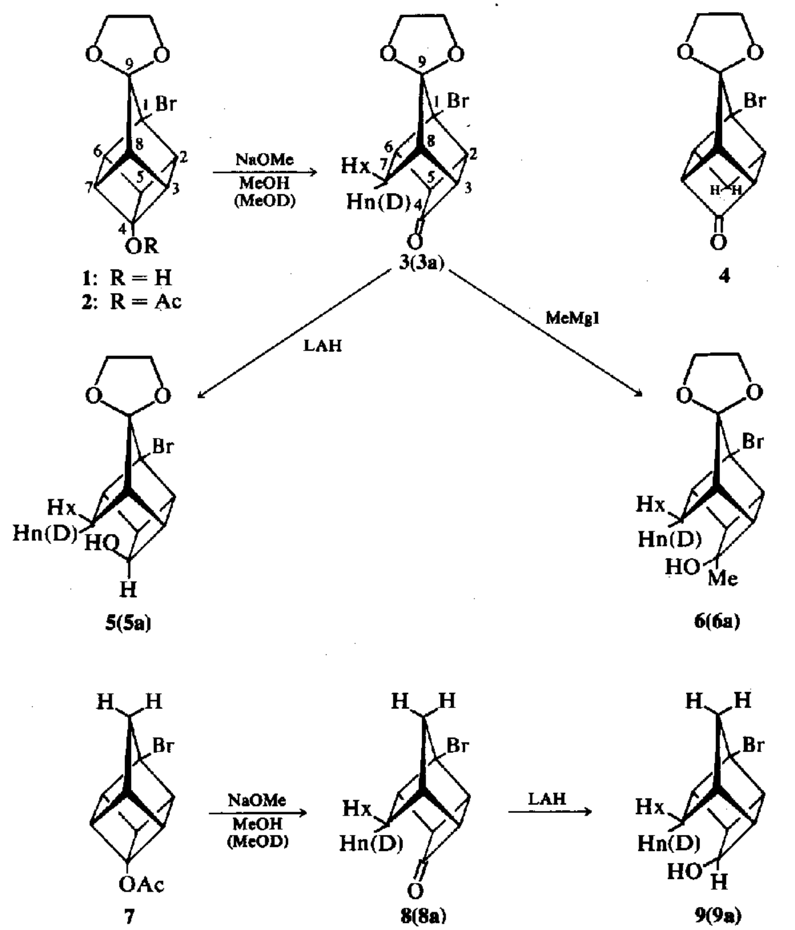
Bridgehead alcohols and amines in highly strained polycyclic systems show a remarkable sensitivity to base as exemplified by the homoketonization reaction of 1-hydroxynortricyclene,[3] a birdcage bridgehead alcohol,[4,5] and an anionic fragmentation of a chlorinated birdcage amine.[6] Apparently, ring strain in these type of compounds has a unique influence on the chemical properties of the hydroxy and amino function.

This paper deals with the homoketonization reaction of some bridgehead cage alcohols which show a diversity in cage strain, *viz* cubane, homocubane and 1,3-bishomocubane alcohols. The synthesis of these alcohols was described in previous parts of these series.[2,7]

The homocubane bridgehead alcohol **1** and its acetate **2** were extremely base labile. Upon treatment with NaOMe in MeOH, alcohol **1** or its acetate **2** reacted almost instantaneously, giving half cage ketone **3** in quantitative yield (Scheme 1). To this ketone which was isomeric with alcohol **1**, structure **3** was assigned on basis of spectral evidence. The IR spectrum shows a C═O stretching frequency at 1765 cm^{-1}, typical for a cyclobutanone. The NMR spectrum (C_6D_6) displays one half of an AB quartet as a doublet of doublets centered at δ 1·30 ppm* ascribed to inside proton H_n. This H_n signal is split by H_x (J ~ 13 Hz) and by H_8 (J ~ 2 Hz). Coupling with H_8 is negligible probably because the dihedral angle between H_n and H_8 is about 90°. The lowfield half of the AB pattern for H_x appears as a broad multiplet centered at δ 2·1 ppm.* This absorption coincides with that of H_8. The ethylene ketal protons appear as an unsymmetrical multiplet between δ 3·41 and 4·0 ppm, while the remaining protons are found at δ 2·4–3·0 ($H_{3,5}$) and δ 3·10–3·40 ($H_{2,6}$) as a complex pattern. The isomeric structure **4** which can be envisioned by scission of the central C_4—C_5 bond, must be rejected on basis of the NMR spectrum, since: (i) a doublet of triplets would be expected for the *endo* proton H_n in **4** as the result of coupling with H_x and the equivalent protons H_2 and H_6, (ii) in the symmetrical ketone **4** the ethylene ketal protons are expected to appear as a symmetrical AA′BB′ absorption,† (iii) the upfield shift for H_8 in **3** as compared with **1** is in agreement with relief of strain around C_8 in **3** (in **4** the congestion around C_8 has hardly changed). Further confirmation of structure **3** was obtained from its behaviour during LAH reduction and from the Grignard reaction with MeMgI. As expected for such half-cage structures,[4] reaction with these reagents proceeds with a high degree of steric approach control to yield exclusively the oxygen-inside alcohols **5** and **6**, respectively. Because of the congestion in the half cage

*In $CDCl_3$, H_n = δ 1·64; H_x = δ 2·11–2·67, see also Experimental.

†However, when a symmetrical absorption is observed it does not necessarily imply that the ketal containing compound has a plain of symmetry.[8]



Scheme 1

alcohols **5** and **6**, the *endo* proton H_n will experience a strong deshielding effect of the OH-function.[9] The spectra of **5** and **6** indeed show the H_n signal at a deshielded position, *viz* as a half of an AB quartet centered at δ 2·64 ppm for **5** and at δ 3·04 ppm for **6**. The outside protons H_x appear as complex multiplets at δ 1·85–2·35 and 2·05–2·45 ppm, respectively. Unequivocal assignment of the H_x and H_n signals was accomplished with deuterium labeling (*vide infra*).

With the structure of **3** resolved, attention was turned to the stereochemistry of the cleavage of the cyclobutane ring. Hence, acetate **2** was treated with NaOMe in MeOD giving mono deuterated ketone **3a** in quantitative yield. The NMR spectrum revealed that deuterium was introduced exclusively (> 96%) at the C_7 *endo* position because of the absence of the AB pattern at δ 1·30 and a simplified two proton absortion for H_x and H_8 at δ 2·1 ppm (the signals of H_2, H_3, H_5, H_6 and the ketal protons remained unchanged). Under the same conditions, treatment of ketone **3** with NaOMe in MeOD did not lead to any H/D exchange. Evidently, homoketonization of **1** is a highly stereospecific process and proceeds with retention (> 96%) of configuration at C_7.

From inspection of molecular models, it became apparent that the bulky ketal group could seriously hamper the approach of the proton donating solvent molecule, *i.e.* methanol, from the *exo*-side and therefore would promote *endo*-attack. For this reason the homoketonization of deketalized acetate **7** was investigated. Treatment of **7** with NaOMe in MeOH at room temperature gave quantitatively the half cage ketone **8**. The IR spectrum shows the characteristic C=O absorption at 1765 cm^{-1}. Unexpectedly, the NMR spectrum did not display the AB pattern for C_7 methylene protons, but instead a narrow, almost unsplit two proton absorption (a degenerated AB pattern) was observed at δ 1·72 ppm for the protons H_n and H_x. Apparently, the *in*side proton H_n in half cage ketones **3** and **8** is not significantly shielded by the C=O function. The difference between the H_xH_n absorption in **3** and **8** is most likely due to a deshielding of H_x in **3** by the anisotropy of the ethylene ketal function and not to the anticipated shielding effect of the C=O group at C_4. The remaining part of the spectrum was entirely consistent with the proposed structure **8**, *viz* the methylene protons at C_9 appear as an AB quartet (J ~ 12 Hz) centered at δ 2·03, confirming the asymetric structure of **8**, and the bridgehead protons H_2, H_3, H_5, H_6 absorb at δ 3·35–3·80 and δ 2·70–3·15 ppm as complex multiplets.

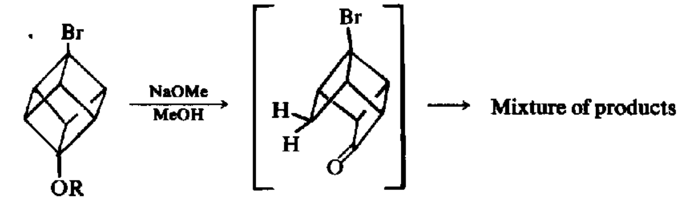
By performing the homoketonization of acetate **7** with NaOMe in MeOD monodeuterated ketone **8a** was obtained in quantitative yield. The NMR spectrum exhibits a one proton absorption at δ 1·55–1·85 ppm for either the *exo* proton H_x or the *endo* proton H_n (the other signals remained unchanged). To differentiate between H_x and H_n, ketone **8** and its monodeuterated form **8a** were reduced with LAH. In both cases exclusive formation of oxygen inside alcohols *viz* **9** and **9a** was observed (Cf. formation of alcohol **5**). The NMR of **9** exhibits one half of an AB quartet (J_{AB} ~ 12 Hz) as doublets (J ~ 1·5 Hz) at δ 2·78 and 2·60 for proton H_n and a doublet of complex multiplets at δ 1·2–1·6 ppm for proton H_x, whereas in the spectrum of **9a** the AB pattern at δ 2·78 and 2·60 was absent and the H_7 proton ($\equiv H_x$) appeared as a simplified multiplet at δ 1·38–1·58 ppm.

Comparison of these data indicates that the H_n proton in **8a** was replaced by D. Hence, the introduction of the ethylene ketal group at C_9 in the homocubane system does not alter the stereochemical course of the homoketonization. The acetate **2** as well as **7** gives exclusively cleavage of the C_4—C_7 bond (or the equivalent C_3—C_4 bond) with a subsequent protonation which is highly stereospecific (> 96% retention of configuration at C_7).

The cubane alcohol **10** and its acetate **11** appeared to be even more sensitive towards base than the homocubane bridgehead alcohols and acetates (Scheme 2). On mild treatment with NaOMe or KOH in MeOH, alcohol **10** and acetate **11** reacted instantly to a complex mixture of cage degradation products. The IR and NMR spectra showed several carbonyl and olefinic absorptions. Attempts to separate these products (GLC and TLC) were unsuccessful. Presumably, the half cage ketone **12** has been formed, but because of the large constraint in the half cage system, subsequent fragmentation will take place readily, leading to mixtures of less strained compounds. Thus far, we were unable to isolate or identify any of these compounds.

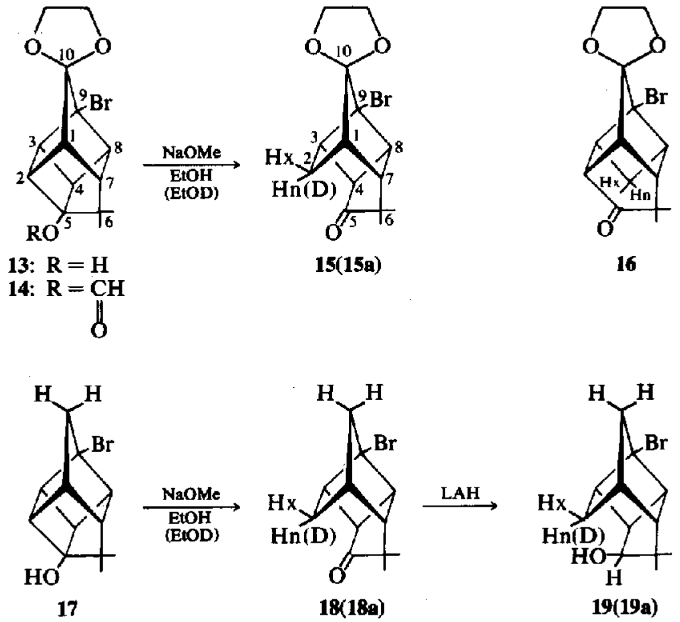
The far less strained 1,3-bishomocubane bridgehead alcohol **13** and formate **14** did not show homoketonization upon treatment with NaOMe in MeOH at room—or even at reflux temperature. However, another increase in reaction temperature was sufficient to bring about the homoketonization reaction. Alcohol **13** or formate **14** gave, when treated with NaOMe in refluxing EtOH, a sole ketone to which structure **15** was assigned (Scheme 3). The IR spectrum shows a C=O absorption at 1730 cm^{-1} indicative of a cyclopentanone. The NMR spectrum ($CDCl_3$) displays one half of an AB pattern as a doublet of doublets (J_1 ~ 13 Hz, J_2 ~ 1 Hz) for the inside proton H_n at δ 1·75 and δ 1·52, a doublet of multiplets (J ~ 13 Hz) for the outside proton H_x centered at δ 2·32, singlets for the Me groups at δ 1·11 and δ 0·94, a complex multiplet for H_1 at δ 2·0, a multiplet for the remaining bridgehead protons at δ 2·58–3·60, and a symmetrical AA′BB′ multiplet[8] for the ethylene ketal function at δ 3·78–4·43 ppm. Although the IR and NMR spectra are consistent with the proposed structure **15**, they can not differentiate between the ketone **15** and its isomer **16**, arising from C_4—C_5 bond cleavage. Unambiguous evidence for structure **15** was obtained from the NMR spectrum of deketalized ketone **18**, which was produced in quantitative yield from alcohol **17**. The outside proton H_x and inside proton H_n in **18** appear as a broad multiplet at δ 1·77. The large down field shift (Δδ ~ 0·6 ppm) observed for H_x in **15** as compared with H_x in **18** is largely due to the magnetic anisotropy of the ethylene ketal function (*vide supra*), and can only be reconciled with structures **15** and **18**, since in half cage ketone **16** no such deshielding effect of the ethylene ketal group on H_x is expected. Evidently, homoketonization of 1,3-bishomocubane alcohols proceeds exclusively by cleavage of the C_2—C_5 bond in the direction of the least strained ketone.

The stereochemistry of the cage opening of alco-



10: R = H
11: R = Ac
12

SCHEME 2



13: R = H
14: R = CHO

15(15a)

16

17

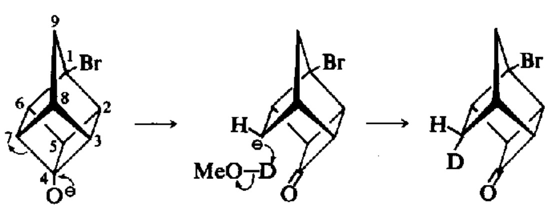
18(18a)

19(19a)

SCHEME 3

hols 13 and 17 was studied by performing the homoketonization with NaOMe in refluxing EtOD (Scheme 3). The position of deuterium in the so-obtained ketones **15a** and **18a** was established to be exclusively *endo* in both cases. The NMR spectrum of **15a** was lacking the H_n signal, while the H_x absorption had a simplified pattern as compared with **15**. Similarly as described for **9a**, the spectrum of the inside alcohol **19a** provides a means to show that deuterium had entered exclusively the *endo* position in **18a**. Thus, the presence of the ethylene ketal function at C_{10} does not alter the stereochemistry of the homoketonization of the 1,3-bishomocubane alcohols.

These homoketonization experiments with the homocubane and 1,3-bishomocubane bridgehead alcohols clearly demonstrate the occurrence of a directional-selective bond cleavage and a strict stereochemical control in the subsequent proton uptake. In Scheme 4 a mechanism for this base induced process is proposed (shown for **20**). The high selectivity in the direction of the bond cleavage is most likely governed by relief in cage strain. Inspection of molecular models indeed confirms that cleavage of the C_4—C_7 (or C_3—C_4) bond in the homocubane skeleton provides more relief of strain than rupture of the central C_4—C_5 bond. Similarly, breaking of the C_2—C_5 bond is most favourable with regard to relief of cage strain in the bis-homocubane system. Two other types of cage compounds, the only ones mentioned in literature so far, *viz* the birdcage alcohol of Howe and Winstein,[4] and the cage amine of Stedman *et al.*,[6] also show a base induced C—C bond cleavage directed to the least strained half cage compound.

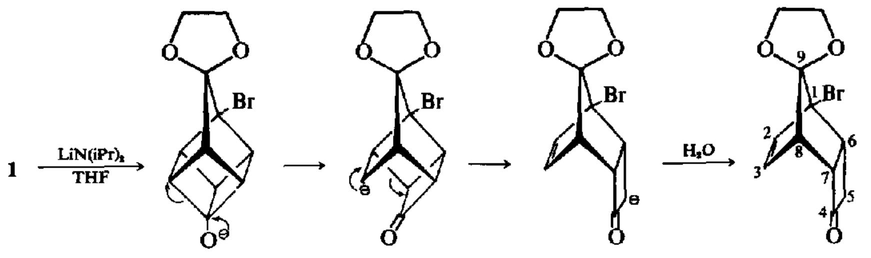


20

8a

SCHEME 4

According to Cram's terminology[10] these cage opening reactions represent examples of an electrophilic substitution at saturated carbon with carbon as leaving group. The stereochemistry of such reactions, particularly the SE_1 type, has extensively been studied for open systems[10] and monocyclic alcohols[10] (inclusive cyclopropanols[11]). It was found that the change in configuration at the carbon of substitution depends on the nature of the solvent (dissociating power and dielectric constant). However, the base-catalyzed ketonization of the strained 1-hydroxynortricyclene to norbornan-2-one takes place with inversion of configuration independent of solvent.[3] Most likely, the views developed for simple systems cannot adequately account for the stereochemical results in their strained counterparts. The stereospecific cleavage of the cyclobutane ring in homocubane and 1,3-bishomocubane takes place with retention of configuration at C_7 and C_2, respectively. In both



SCHEME 5

cases proton uptake occurs from the *endo*-side of the molecule, even in the case of bishomocubane where the *endo* approach of the proton donating EtOH molecule might be hindered by the *gem* dimethyl group at C_6. This stereospecificity requires either that the cleavage reaction produces a non-inverting carbanion or that the proton donor is incorporated in the transition state of the bond cleavage (concerted process). The very high degree of stereospecificity observed in these cage cleavage reactions argues against the intermediacy of free carbanions. Carbanion mechanisms involving preferential *endo*-protonation because the departing carbonyl group gives the intermediate carbanion a polar and non-polar face[12,13] or generation of an energetically unfavourable ion pair during *exo*-protonation,[12,13] are in our opinion too subtle to explain the exclusive retention of configuration. Cyclobutane ring opening in other cage molecules during homoketonization reactions was also found to occur very predominantly with retention, *viz* for a birdcage amine[6] and for 7-phenyltricyclo-[3.2.0.0^{2,6}]heptan-7-ol.[13] Opening of a cyclopentane ring in 3,7-dimethyl tricyclo[3.3.0.0^{3,7}]octan-1-ol[12] showed 98% net retention of configuration during the base-induced fragmentation process independent of solvent. We are inclined to believe that the stereochemistry of 90% inversion for the homoketonization of Nickon's nortricyclanol,[3] which is opposite to the cases described above, must be attributed to the special nature of the cyclopropane ring present in this system.

More information about the fate of the presumed carbanion was obtained when the reaction with base was conducted under aprotic conditions. Accordingly, homocubane alcohol **1** was treated with $LiN(iPr)_2$ in THF (Scheme 5). A sole product was obtained to which structure **21*** was assigned. The IR spectrum shows a C=O absorption at 1785 cm^{-1}, typical for a cyclobutanone, and a weak olefinic C—H band at 3080 cm^{-1}. The NMR spectrum displays a narrow multiplet at δ 6·17 ppm for the olefinic protons H_2 and H_3, an unsymmetrical multiplet at δ 3·6–4·35 ppm for the ethylene ketal group which coincides with one of the bridgehead protons, and a complex multiplet between δ 2·4 and δ 3·3 ppm for the remaining protons. Similar cage fragmentation products were observed in the homoallylic type rearrangement of a 4-homocubane methylcyanide[1] and a 4-homocubane methyl sulfone.[14] A mechanistic pathway for the base induced cage fragmentation reaction is outlined in Scheme 5. Evidently, under the applied aprotic conditions the homoketonization does not stop at the stage of the half cage system, but another C—C bond is broken producing a less congested carbanion. Bishomocubane alcohol **13** on treatment with $LiN(iPr)_2$ in THF or dioxane did not lead to anionic fragmentation neither at room temperature nor in refluxing solvent. Apparently under aprotic conditions the reaction conditions need to be more drastic to achieve cage fragmentation than with a protic solvent.

This extended fragmentation to **21** provides a good means to gather some additional evidence for the concerted mechanism proposed for the homoketonization under protic conditions. When a free carbanion is a true intermediate one would expect at least some further fragmentation of the homocubane alcohol to a structure like **21** when such fragmentation is placed in a fair competition with protonation. However, by performing the homoketonization of **1** with NaOMe as base in dioxane or acetonitril as solvents, containing a trace of MeOH, a quantitative yield of the half-cage ketone **3** was isolated. This result substantially supports a synchronous mechanism for the homoketonization reaction.

*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.

EXPERIMENTAL

IR spectra were taken on a Perkin Elmer 125 or 257 grating spectrometer. NMR spectra were recorded on a Varian A60 or T60 spectrometer, using TMS as internal standard. All m.ps are uncorrected and determined on a Kofler hot stage. Elemental analyses were carried out in duplicate (their average values are reported), in the micro analytical department of the University at Groningen under supervision of Mr. W. M. Hazenberg.

1-*Bromotetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonan*-4,9-*dione* 9-*ethylene ketal* (**3**). NaOMe (0·05 g, 0·92 mmole) was added to a stirred soln of acetate **2** (0·1 g, 0·3 mmole) in MeOH (5 ml). After stirring at room temp for 1 hr, MeOH was removed *in vacuo*, the residue diluted with water and ether extracted. The ether layer was dried ($MgSO_4$) and the solvent evaporated to give ketone **3** (0·08 g, ~ 100%) as a crystalline solid. Recrystallization from hexane gave a pure sample, m.p. 75–77°; IR ν_{max}^{KBr} 1765 (C=O) cm^{-1}; NMR (C_6D_6) δ 3·41–4·0 (m, 4H, ketal group), 2·4–3·4 (m, 4H), 2·1 (m, 2H, protons H_x and H_8), 1·30 (d, J_1 ~ 13 Hz, J_2 ~ 2 Hz, 1H, proton H_n). NMR ($CDCl_3$) 3·83–4·35 (symm. m., 4H, ketal group), 3·53–3·90 (m, 2H, H_2 and H_6), 2·90–3·26 (m, 2H, H_3 and H_5), 2·11–2·67 (m, 2H, H_x and H_8), 1·64 (d, J_1 ~ 13 Hz, J_2 ~ 2 Hz, 1 H, proton H_n). *m/e* 271 (M^+, 1 Br). (Found: C, 48·37; H, 4·05; Br, 29·30; Calc. for $C_{11}H_{11}BrO_3$: C, 48·73; H, 4·09; Br, 29·48%). The same result was obtained when alcohol **1** was used as the starting material. 1-*Bromo*-7-endo-*deuteriotetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonan-4,9-dione 9-ethylene ketal* (**3a**) was prepared as described above using MeOD instead of MeOH; NMR (C_6D_6) δ 3·41–4·0 (m, 4 H, ketal group), 2·4–3·4 (m, 4 H), 2·1 (m, 2 H, protons H_x and H_8). *m/e* 272 (M^+, 1 Br).

1-*Bromo*-4-endo-*hydroxytetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonan-9-one ethylene ketal* (**5**). A soln of ketone **3** (0·1 g, 0·4 mmole) in anhyd ether (5 ml) was added to a soln of LAH (0·015 g, 0·4 mmole) in ether (5 ml). After stirring overnight, the mixture was diluted with water and ether extracted. The ether layer was dried ($MgSO_4$) and concentrated to give crude alcohol **5** (0·08 g, 80%). Recrystallization from hexane gave an analytically pure sample, m.p. 87–89·5°; IR ν_{max}^{KBr} 3300 (O—H) cm^{-1}; NMR ($CDCl_3$) δ 3·75–4·30 (m, 5H, ethylene ketal group and proton H_4), 2·4–3·4 (m, 4H), 2·72 and 2·56 (d, J_1 ~ 13 Hz, J_2 ~ 1 Hz, one half of an AB quartet, 1H, proton H_n), 1·85–2·35 (m, 2H, protons H_x and H_8), 1·80 (s, 1H, OH). (Found: C, 48·34; H, 4·92; Br, 28·85; Calc. for $C_{11}H_{13}BrO_3$: C, 48·37; H 4·80; Br, 29·26%). 1-*Bromo*-7-endo-*deuterio*-4-endo-*hydroxytetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonan-9-one ethylene ketal* (**5a**) was prepared as described above using monodeuterated ketone **3a** as the starting material; NMR ($CDCl_3$) δ 3·75–4·40 (m, 5H, ketal group and proton H_4), 2·40–3·40 (m, 4H), 2·30 (m, 1H, proton H_8), 2·10 (m, 1H, proton H_x), 2·0 (s, 1H, OH).

1-*Bromo*-4-endo-*hydroxy*-4-exo-*methyltetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonan-9-one ethylene ketal* (**6**) was prepared as described above using excess MeMgI instead of LAH. Ketone **3** gave **6** in 76% yield, m.p. 123–125° (hexane); IR ν_{max}^{KBr} 3250 (O—H) cm^{-1}; NMR (C_6D_6) δ 3·25–4·05 (m, 4H, ketal group), 3·12 and 2·95 (d, J_1 ~ 12 Hz, J_2 ~ 2 Hz, one half of an AB pattern, 1H, proton H_n), 2·45–2·90 (m, 4H), 2·05–2·45 (m, 2H, protons H_x and H_8), 0·85 (s, 3H, CH_3). (Found: C, 50·19; H, 5·27; Br, 27·60; Calc. for $C_{12}H_{15}BrO_3$: C, 50·19; H, 5·27; Br, 27·83%). 1-*Bromo*-7-endo-*deuterio*-4-endo-*hydroxy*-4-exo-*methyltetracyclo*[4.3.0.0.0^{2,5}.0^{3,8}]*nonan-9-one ethylene ketal* (**6a**) was prepared in the same way, utilizing monodeuterated ketone **3a** as starting material; NMR (C_6D_6) δ 3·25–4·05 (m, 4H, ketal group), 2·40–3·00 (m, 4H), 2·05–2·30 (m, 2H, H_x and H_8), 0·86 (s, 3H, CH_3).

1-*Bromotetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonan-4-one* (**8**). The same procedure as for the preparation of ketone **3** was used. A quantitative yield of crude **8** was obtained from acetate **7**. Recrystallization from hexane gave a pure sample: m.p. 54–56°; IR ν_{max}^{KBr} 1765 (broad C=O) cm^{-1}; NMR ($CDCl_3$) δ 3·35–3·80 (m, 2H), 2·70–3·15 (m, 3H), 2·03 (AB quartet, J_1 ~ 12 Hz, J_2 ~ 1 Hz, 2H, methylene protons at C_9); 1·72 (m, 2H, protons H_x and H_n). *m/e* 213 (M^+, 1 Br). 1-*Bromo*-7-endo-*deuteriotetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonan-4-one* (**8a**) was prepared as described for **8** using MeOD instead of MeOH; NMR ($CDCl_3$) δ 3·35–3·85 (m, 2H), 2·75–3·20 (m, 3H), 2·04 (AB quartet, J_1 ~ 12 Hz, J_2 ~ 1 Hz; 2H, methylene protons at C_9), 1·55–1·85 (m, 1H, proton H_x). (Found: C, 50·31; H, 4·17; Br, 37·19; Calc. for C_9H_8DBrO: C, 50·51; H, 4·25; Br, 37·34%).

1-*Bromo*-4-endo-*hydroxytetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonane* (**9**). The same procedure as for the preparation of alcohol **5** was used. Ketone **8** gave alcohol **9** as an oil in 90% yield. Crystallization from hexane gave an analytically pure sample, m.p. 72–75°; IR ν_{max}^{KBr} 3280 (O—H) cm^{-1}; NMR ($CDCl_3$) δ 4·12 (t, J ~ 6 Hz, 1H, proton H_4), 2·3–3·3 (m, 5H), 2·78 and 2·60 (d, one half of an AB quartet, J_1 ~ 12 Hz, J_2 ~ 1·5 Hz, 1H, proton H_n), 1·80 (AB quartet, J_1 ~ 11 Hz, J_2 ~ 1 Hz, 2H, methylene protons at C_9), 1·83 (s, 1H, OH), 1·2–1·6 (m, 1H, proton H_x). (Found: C, 50·65; H, 5·29; Br, 36·57; Calc. for $C_9H_{11}BrO$: C, 50·25; H, 5·16; Br, 37·15%). 1-*Bromo*-7-endo-*deuterio*-4-endo-*hydroxytetracyclo*[4.3.0.0^{2,5}.0^{3,8}]*nonane* (**9a**) was prepared as described above, using monodeuterated ketone **8a** as starting material; NMR ($CDCl_3$) δ 4·12 (t, J ~ 6 Hz, 1H, proton H_4), 2·3–3·3 (m, 5H), 1·80 (AB quartet, J_1 ~ 11 Hz, J_2 ~ 1·5 Hz, 2H, methylene protons at C_9), 1·84 (s, 1H, OH), 1·38–1·58 (m, 1H, proton H_x).

6,6-*Dimethyl*-9-*bromotetracyclo*[5.3.0.0^{3,9}.0^{4,8}]*decan*-5,10-*dione* 10-*ethylene ketal* (**15**). A soln of formate **14** (0·1 g, 0·3 mmole) in dry EtOH (10 ml) containing NaOMe (0·5 g, 9 mmole) was heated under reflux for 16 hr. The EtOH was removed *in vacuo*, the residue diluted with water and ether extracted. The ether layer was dried ($MgSO_4$) and the solvent evaporated affording half cage ketone **15** (0·09 g, 95%) as a crystalline solid. Recrystallization from hexane gave a pure sample, m.p. 95–96°; IR ν_{max}^{KBr} 1730 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 3·78–4·43 (sym m., 4H, ketal group), 2·58–3·60 (m, 4H), 1·83–2·58 (m, 2H, protons H_x and H_1), 1·75 and 1·52 (d, J_1 ~ 13 Hz, J_2 ~ 1 Hz, one part of an AB quartet, 1H, proton H_n), 1·11 (s, 3H, Me), 0·94 (s, 3H, CH_3); *m/e* 313 (M^+, 1 Br). (Found: C, 53·76; H, 5·66; Br, 25·77; Calc. for $C_{14}H_{17}BrO_3$: C, 53·69; H, 5·47; Br, 25·51%). 6,6-*Dimethyl*-9-*bromo*-2-endo-*deuteriotetracyclo*[5.3.0.0^{3,9}.0^{4,8}]*decan*-5,10-*dione* 10-*ethylene ketal* (**15a**) was prepared as described for **15** using EtOD instead of EtOH; NMR ($CDCl_3$) δ 3·80–4·45 (sym m. 4H, ketal group), 2·6–3·5 (m, 4H), 2·3 (m, 1H, proton H_x), 2·02 (m, 1H, proton H_1), 1·1 (s, 3H, CH_3), 0·94 (s, 3H, CH_3).

6,6-*Dimethyl*-9-*bromo*-5-*hydroxypentacyclo*[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]*decane* (**17**) was prepared as described previously,[2] utilizing dimethyl 4-(1-bromopentacyclo-[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]nonane) carbinol as the starting material. An 80% yield of bridgehead alcohol **17** was obtained. Recrystallization from hexane gave a pure sample, m.p. 66–69°; IR ν_{max}^{KBr} 3300 (OH) cm^{-1}; NMR ($CDCl_3$) δ 2·5–3·1 (m, 5H), 2·0–2·25 (m, 1H), 1·93 (s, 2H, methylene protons at C_{10}), 1·67 (s, 1 H, OH), 0·90 (s, 3 H, Me), 0·72 (s, 3 H, Me). (Found: C, 56·04; H, 6·00; Br, 30·97; Calc. for $C_{12}H_{15}BrO$: C, 56·48; H, 5·93; Br, 31·32%).

6,6-*Dimethyl*-9-*bromotetracyclo*[5.3.0.0^{3,9}.0^{4,8}]*decan*-5-*one* (**18**). The same procedure as for the preparation of ketone **15** was used. Alcohol **17** afforded ketone **18** in almost quantitative yield. Recrystallization from hexane gave an analytically pure sample: m.p. 81–82·5°; IR ν_{max}^{KBr} 1730 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2·25–3·40 (m, 5H), 1·98 (AB quartet, J_1 ~ 11 Hz, J_2 ~ 1·5 Hz, 2H, methylene protons at C_{10}), 1·77 (m, 2H, protons H_x and H_n), 1·11 (s, 3H, CH_3), 0·92 (s, 3H, CH_3) *m/e* 255 (M^+, 1 Br). (Found: C, 56·36; H, 5·92; Br. 31·18; Calc. for $C_{12}H_{15}BrO$: C, 56·48; H, 5·93; Br, 31·32%). 6,6-*Dimethyl*-9-*bromo*-2-endo-*deuteriotetracyclo*[5.3.0.0^{3,9}.0^{4,8}]*decan*-

5-*one* (**18a**) was prepared as described for **18**, using EtOD instead of EtOH; NMR ($CDCl_3$) δ 2·25–3·40 (m, 5 H), 1·95 (AB quartet, $J_1 \sim 11$ Hz, $J_2 \sim 1·5$ Hz, 2H, methylene protons at C_{10}), 1·58–1·83 (m, 1H, proton H_x), 1·09 (s, 3H, CH_3), 0·90 (s, 3H, CH_3).

6,6-*Dimethyl*-9-*bromo*-5-endo-*hydroxytetracyclo*[5.3.0.0^{3,9}.0^{4,8}]*decane* (**19**). The same procedure as for the preparation of alcohol **5** was used. Ketone **18** gave crude alcohol **19** in 90% yield. Recrystallization from hexane and subsequent sublimation (80°/12 mm) afforded an analytically pure sample: m.p. 84–85°; IR ν_{max}^{KBr} 3400 (O—H) cm^{-1}; NMR (C_6D_6) δ 3·4 (d, J ~ 6 Hz, 1H, proton H_5), 2·2–3·2 (m, 3H), 2·55 and 2·78 (d, one half of an AB quartet, J ~ 12 Hz, 1H, proton H_n), 1·8 (m, 4H, cage protons and methylene protons at C_{10}), 1·3 (m, 1H, proton H_x), 0·85 (s, 3H, CH_3), 0·64 (s, 3H, Me). (Found: C, 56·71; H, 6·88; Br, 30·70; Calc. for $C_{12}H_{17}BrO$: C, 56·04; H, 6·67; Br, 31·07%). 6,6-*Dimethyl*-9-*bromo*-2-endo-*deuterio*-5-endo-*hydroxytetracyclo*[5.3.0.0^{3,9}.0^{4,8}]*decane* (**19a**) was prepared in the same way, utilizing monodeuterated ketone (**18a**) as starting material; NMR (C_6D_6) δ 3·4 (d, J ~ 6 Hz, 1H, proton H_5), 2·2–3·2 (m, 3H), 1·8 (m, 4H, cage protons and methylene protons at C_{10}), 1·3 (m, 1H, proton H_x).

1-*Bromotricyclo*[4.2.1.0^{2,5}]*non*-7-*ene*-4,9-*dione* 9-*ethylene ketal* (**21**). To a stirred ice-cooled soln of diisopropylamine (0·4 g, 4 mmole) in THF (5 ml) was added (N_2 atmosphere) 1·5 ml of 2N n-BuLi in hexane. After 15 min a soln of alcohol **1** (0·4 g, 1·5 mmole) in THF (5 ml) was added gradually. After stirring at room temp for 1 hr, water was added and the mixture ether extracted. The extracts were washed with diluted HCl aq and dried ($MgSO_4$). Solvent was removed yielding crude **21** (0·23 g, 58%) as an oil. Crystallization from hexane and subsequent sublimation (100°/12 mm) afforded a pure sample, m.p. 98–102°; IR ν_{max}^{KBr} 3080 (C=CH), 1785 (C=O) cm^{-1}; NMR (CCl_4) δ 6·17 (d, degenerated AB quartet, 2H, protons H_7 and H_8), 3·6–4·35 (m, 5H, ethylene ketal protons and one of the ring protons), 2·4–3·3 (m, 4H). *m/e* 271 (M^+, 1 Br), 149 (M—Br—CH_2=C=O). (Found: C, 48·78; H, 4·24; Br, 28·87; Calc. for $C_{11}H_{11}BrO_3$: C, 48·73; H, 4·09; Br, 29·48%).

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