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CHEMISTRY OF STRAINED POLYCYCLIC COMPOUNDS—III[1,2]

SYNTHESIS OF CUBANE AND HOMOCUBANE ALCOHOLS

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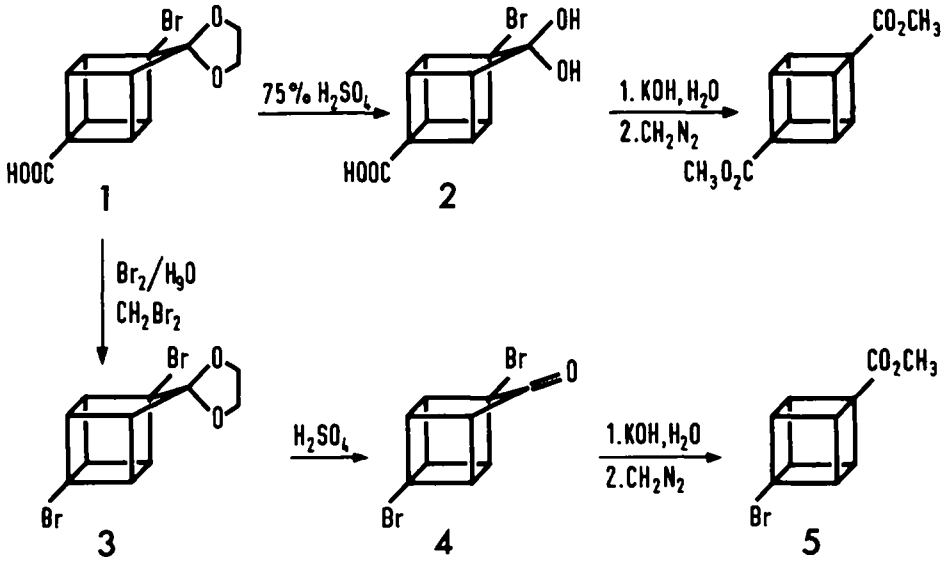
Abstract—The synthesis of three bridgehead alcohols, *viz.* 1-bromo-4-hydroxypentacyclo[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]nonan-9-one ethylene ketal (**8**), 1-bromo-4-hydroxypentacyclo[4.3.0.0.^{2,5}.0^{3,8}.0^{4,7}]nonane (**18**) and 1-bromo-4-hydroxypentacyclo[4.2.0.0^{2,5}.0^{3,8}.0^{4,7}]octane (**24**) is described. Two routes were considered: solvolysis of the corresponding acetates and deamination of the bridgehead amines. The deamination of homocubane 4-amines **11** and **15**, and of cubane amine **23** has been studied under various conditions. An improved cage-contraction of homocubane derivatives to substituted cubanes is described. Despite the increase in ring strain cubane alcohol **24** appeared to be more stable than homocubane alcohols **8** and **18**.

RECENTLY we reported[2] that a homocubane bridgehead alcohol undergoes an interesting homoketonization reaction under basic conditions. In order to study this intriguing phenomenon in more detail, in particular the influence of the cage strain, some cage alcohols were required which show a diversity in strain energy. It should be mentioned that an increase in cage strain in these bridgehead alcohols most likely involves increased thermal lability. This paper deals with the synthesis of three cage alcohols, *viz.* the homocubane alcohols **8** and **18**, and the cubane alcohol **24**.

For the preparation of the cage system we chose the method described by Eaton and Cole.[3] The recent modification reported by Chapman *et al.*[4] proved to be a great practical improvement for the preparation of the homocubane 4-carboxylic acid **1**. The conversion of the homocubane system into a cubane skeleton deserves some comment, because of the difficulties encountered in the cage-contraction step. Chapman *et al.*[4] reported a yield of 10% for this step when the 1-bromo-homocubanone-4-carboxylic acid was used as starting material and 50% KOHaq as base. We found the yield can be doubled (20–25%) by taking the hydrate **2** instead of the ketone as starting material. Apparently this *gem*-diol structure facilitates the semi-benzilic acid rearrangement in this case. A still higher yield (45%) was obtained in this ring contraction step when dibromoketone **4** was used as cubane precursor. This dibromoketone was prepared *via* a Cristol and Firth modification[5] of the Hunsdiecker reaction (Scheme I).

The cage-contraction reaction with 1-bromohomocuban-9-ones having an H[6] or an Me in the 4-position also proceeds much better than that of the carboxylic acid **2** (yields of 45 and 60%, respectively). It is interesting to note that this smooth course of the ring-contraction reaction parallels the relative ease by which the *gem*-diols of the corresponding homocuban-9-ones can be dehydrated to the free ketones.

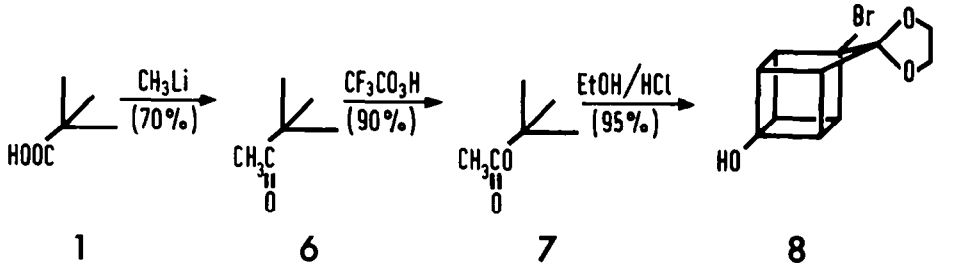
* Part of this work was carried out at the University at Groningen.



SCHEME I

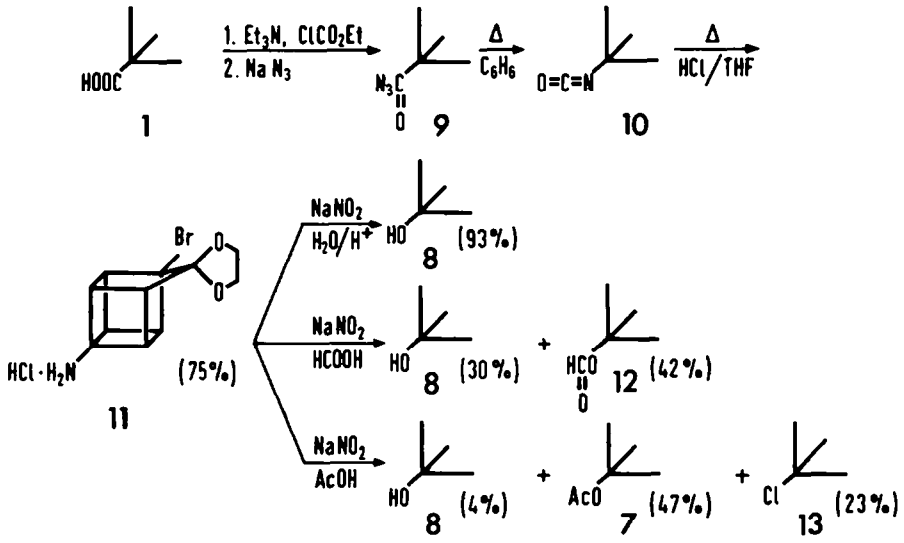
The use of NaOMe (25% solution in MeOH) as base in the Favorskii reaction, gave exclusive reduction to homocubane-9-alcohols (yields of about 50%), no cubane derivative could be isolated or even be detected.

For the homocubane alcohol **8** two approaches were considered, *viz.* conversion of the acetate **7** (Scheme II) and deamination of the amino compound **11** (Scheme III).



SCHEME II

Treatment of **1** with MeLi gave the methyl ketone **6**, which was converted to acetate **7** by a Baeyer–Villiger oxidation with trifluoroperacetic acid. Interestingly, only migration of the cage moiety was observed. Acid catalyzed transesterification of **7** in EtOH gave desired alcohol **8** in almost quantitative yield. Hydrolysis of **7** in dilute HClaq resulted in a mixture of five products of which alcohol **8** dominated. In the presence of base alcohol **8** and its acetate undergo a highly fascinating homoketonization reaction.[2] Pure alcohol **8** is quite stable, on heating in benzene at 55° for 7 hr no noticeable decomposition was observed. Alcohol **8** was characterized by an OH absorption in the IR spectrum at 3400 cm^{-1} and by its NMR spectrum in C_6D_6, which displays a symmetrical multiplet for the ethylene ketal group at δ

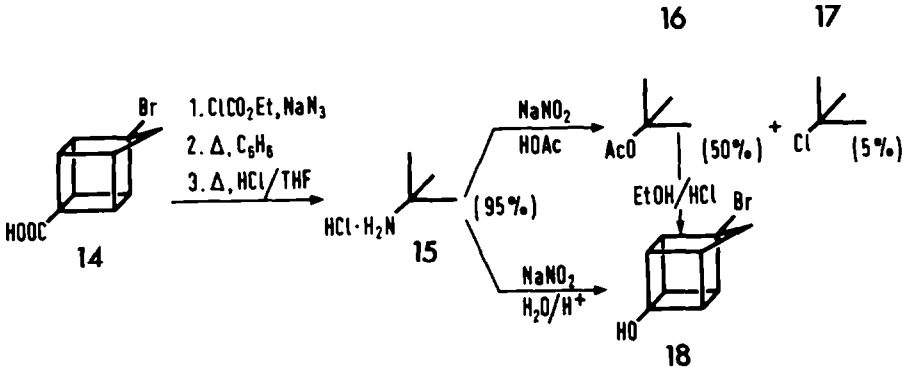


SCHEME III

3·35–4·08 (4 H), a multiplet at δ 3·15–3·38 (5 H) for the cage protons at $C_{2,3,5,6,7}$ and a multiplet at δ 2·55–2·85 (1 H) for the cage proton at C_8.[7] Treatment of **8** with acetylchloride gave acetate **7**, showing unambiguously that the cage skeleton was retained during acid solvolysis.

The starting material for the second approach *i.e.* the homocubane 4-amine hydrochloride **11** could readily be obtained by a Curtius rearrangement of carbonyl-azide **9** (Scheme III). This azide was prepared in high yield by using the method of Weinstock.[8] Attempts to prepare azide **9** by diazotation of the corresponding hydrazide, failed. The free homocubyl amine, obtained from its HCl salt **11** by treatment with aqueous base, is a reasonably stable compound at room temperature. Deamination of **11** was studied under three different conditions (Scheme III). Diazotation with $NaNO_2$ in water at 0° gave, after careful work-up, alcohol **8** in 93% yield. The products obtained in AcOH and HCOOH as the reaction medium, are indicated in Scheme III. These products are typical for an ionic deamination process. Especially the formation of chloride **13** can only be reconciled by an ionic mechanism. The interesting free bridgehead carbonium ion is probably not formed, but the reaction can possibly be best described as a displacement in which the charge separation is minimized. Our results are in sharp contrast with those of Scherer and Lunt[9] on the deamination of 4-amino nonachloropentacyclo[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$] nonane for which they propose a radical pathway. It is possible that in their case a "positive" bridgehead intermediate is strongly destabilized by the electron withdrawing effect of the nine chlorine atoms, making a free radical path for the decomposition of the bridgehead diazonium salt energetically more attractive.

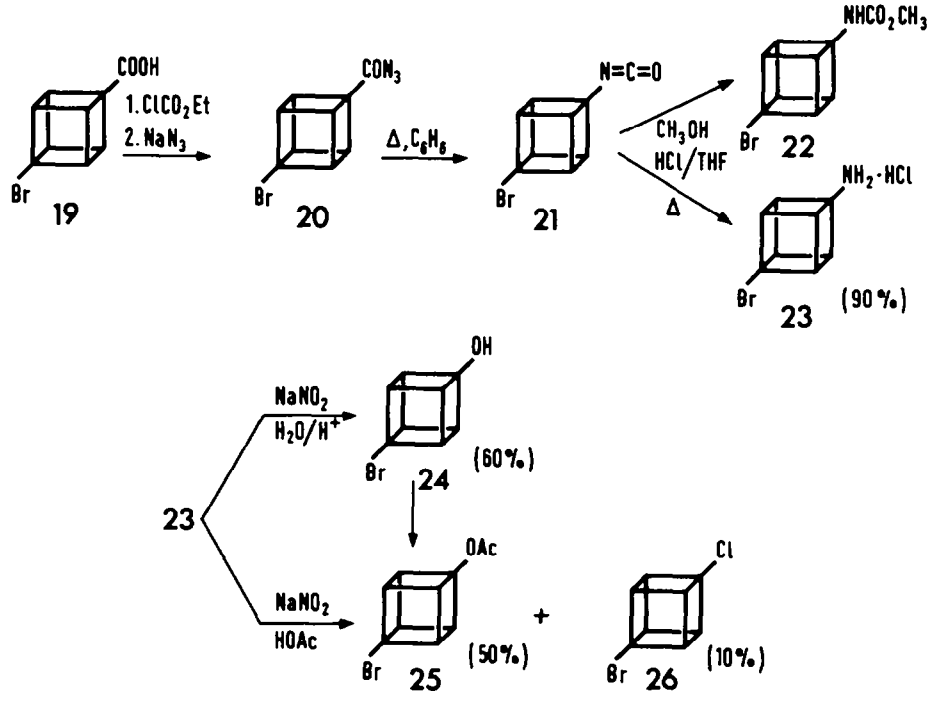
The reaction sequence given in Scheme III was also used to prepare acetate **16** (Scheme IV). Direct conversion of **7** to **16** cannot be realized because of the extreme acid conditions required for the hydrolysis of the ketal function. The ketone function in **2** (as *gem*-diol) could be reduced by the Huong-Minlon modification of the



SCHEME IV

Wolff–Kishner reaction. Alcohol **18** could not be obtained in a pure state by direct deamination of amine **15** in diluted HCl: a mixture of the alcohol and several unidentified and unseparable cage degradation products was obtained. However, acid catalyzed ethanolysis of acetate **16** gave alcohol **18** in quantitative yield. Its structure was established by IR and NMR spectroscopy and by conversion to acetate **16** by treatment with acetyl chloride.

For the preparation of cubane alcohol **24** essentially the same route (Scheme V)



SCHEME V

was followed as for the synthesis of the homocubane alcohols. The carbonyl azide **20**, obtained in almost quantitative yield from acid **19** was converted into the isocyanate **21**, which on treatment with HCl in THF yielded 90% of 1-bromo-cubane 4-amine hydrochloride **23**. The isocyanate (**21**) gave urethane **22** upon treatment with MeOH. The free cubyl amine appeared to be very unstable at room temperature. On standing a deep red colour developed and basic gases escaped from the oily amine. Deamination of the cubane amino hydrochloride **23** was carried out in diluted HCl aq at 0°. After usual work up, a crystalline solid was obtained, which after two recrystallizations from hexane proved to be cubane alcohol **24**. The IR spectrum shows a broad OH absorption at 3100 cm^{-1}. Its NMR spectrum displays a singlet at δ 4·05 for the six cage protons and a broad singlet at δ 3·15 for the OH proton (as shown by a deuterium exchange experiment). One singlet for the six cage protons is not unexpected, because the shielding constants of an OH group and a bromine atom are almost the same.[10] The structure of cubane alcohol **24** was proved unequivocally by conversion of the alcohol into acetate **25** by treatment with acetylchloride in ether. The same acetate was prepared by diazotation of the cubane amine hydrochloride **23** in AcOH (Scheme V). During the diazotation of **23** a mixture of the cubane chloride **26** and the cubane acetate **25** was obtained which could be separated by column chromatography on silica (yield 10% and 50% respectively). Unexpectedly this cubane alcohol is quite stable at room temperature and can be crystallized from hexane. It decomposes just above 100°. Under neutral conditions it was even more stable than the homocubane alcohols **8** and **18**, despite the increase in cage strain. However, under slightly basic conditions the cubane alcohol reacts much faster than the homocubane alcohols giving rise to a number of cage-opened products.[11]

EXPERIMENTAL

IR spectra were taken on a Perkin–Elmer 125 grating spectrometer. NMR spectra were recorded on a Varian A60 spectrometer, using TMS as internal standard. All m.ps are uncorrected and determined on a Kofler hot stage. Elemental analyses were carried out in the Microanalytical Department of the University at Groningen under supervision of Mr. W. M. Hazenberg.

1-*Bromopentacyclo*[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*nonan-9-one ethylene ketal 4-carboxylic acid* (**1**) was prepared in 70–80% yield as described by Key,[6] m.p. 187–189°.

1,4-*Dibromopentacyclo*[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*nonan-9-one ethylene ketal* (**3**). A solution of bromine (0·8 g, 5 mmole) in CH_2Br_2 (10 ml) was added dropwise to a solution of acid **1** (1·0 g, 3·3 mmole) in boiling CH_2Br_2 (25 ml) containing red HgO (0·8 g, 3·7 mmole). When the addition was completed, the mixture was heated under reflux for 3 hr, cooled to room temp and filtered. The CH_2Br_2 was removed *in vacuo* giving a brown solid which was hexane extracted. Evaporation of hexane afforded dibromide **3** (0·9 g, 82%) as crystalline white solid. Recrystallization from EtOH gave a pure sample, m.p. 143–144° (lit.[6] m.p. 138–141°). IR ν_{max}^{KBr} 3020, 1290 and 1075 cm^{-1}: NMR ($CDCl_3$) δ 3·80–4·40 (sym.m., 4H, ketal group), 3·60–3·85 (m, 5H), 2·95–3·28 (m, 1H, proton at C_8): *m/e* 334 (M^+, 2Br). Correct C, H, Br analysis for $C_{11}H_{10}Br_2O_2$.

1,4-*Dibromopentacyclo*[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*nonan-9-one* (**4**). Dibromide **3** (0·2 g, 0·61 mmole) was added in small portions to a stirred mixture of conc H_2SO_4 (27 ml) and H_2O (15 ml). After three days, the solution was poured onto crushed ice, ether extracted and the ether extracts dried ($MgSO_4$). Solvent was removed yielding ketone **4** (0·17 g, 97%). Crystallization from hexane and sublimation (100°/0·1 mm) gave an analytically pure sample, m.p. 143–144°, (lit.[6] m.p. 132–134°): IR ν_{max}^{KBr} 3040, 1755 (shoulder at 1785, C=O) cm^{-1}: NMR ($CDCl_3$) δ 3·60–4·20 (m, 5H), 3·20–3·55 (m, 1H, proton at C_8): *m/e* 290 (M^+ 2Br). Correct analysis (C, H, Br) for $C_9H_6Br_2O$.

Methyl 1-*Bromopentacyclo*[4.2.0.0^{2,5}.0^{3,8}.0^{4,7}]*octane* 4-*carboxylate* (**5**). A solution of ketone **4** (1·0 g, 3·5 mmole) in KOH aq (25 ml of 25% w/w) was heated under reflux for 4 hr. After cooling to room temp. water was added and the solution extracted with ether. The water layer was acidified with dilute HCl, ether extracted and the extracts dried ($MgSO_4$). Solvent was removed yielding 1-bromocubane 4-carboxylic acid (**19**) as a white solid. This was treated with ethereal CH_2N_2 affording the ester **5** (0·37 g, 48%). An analytically pure sample was obtained by column chromatography over silica by elution with hexane/benzene (1 : 1), m.p. 119–121°. IR ν_{max}^{KBr} 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 4·28 (s, 6H), 3·70 (s, 3H, OMe); *m/e* 241 (M^+, 1Br). (Found: C, 49·65; H, 3·88; Br, 33·11. Calc. for $C_{10}H_9BrO_2$: C, 49·82; H, 3·76; Br, 33·14%).

1-*Bromo*-4-*acetylpentacyclo*[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]*nonan*-9-*one ethylene ketal* (**6**). A slurry of carboxylic acid **1** (5·5 g, 0·018 mole) in anhyd ether (175 ml) was added gradually to an ice-cooled solution of MeLi in ether. After stirring for 2 hr, the mixture was diluted with water and extracted with ether. The ether layer was dried ($MgSO_4$) and concentrated to give crude ketone **6** (4·6 g, 85%). Two recrystallizations from hexane furnished an analytically pure sample, m.p. 100–102°. IR ν_{max}^{KBr} 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 3·85–4·45 (sym.m., 4H, ketal group), 3·40–3·90 (m, 5H), 2·85–3·15 (m, 1H, proton at C_8), 2·09 (s, 3H, Me); *m/e* 297 (M^+, 1 Br). (Found: C, 52·55; H, 4·53; Br, 26·75; Calc. for $C_{13}H_{13}BrO_3$: C, 52·55; H, 4·41; Br, 26·89%). A semicarbazone was formed in the usual way. Recrystallization from EtOH gave a pure sample, m.p. > 210°, dec. Analysis correct for C, H, Br and N.

1-*Bromopentacyclo*[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]*nonan*-9-*one ethylene ketal* 4-*acetate* (**7**). A solution of trifluoroperacetic acid was prepared by mixing trifluoroacetic anhydride (3·40 ml) with 100% H_2O_2 (0·5 ml) and CH_2Cl_2 (6·60 ml). The resulting peracid solution was added dropwise to a stirred solution of ketone **6** (1·0 g, 3·4 mmole), anhydrous Na_2HPO_4 (4·0 g) and CH_2Cl_2 (20 ml). The mixture was stirred and refluxed for 10 hr, filtered and the inorganic salts washed thoroughly with CH_2Cl_2. The organic solution was dried ($MgSO_4$) and the solvent evaporated to give acetate **7** (1·0 g, 94%), (containing some trifluoroacetate as indicated by an additional carbonyl band at 1790 cm^{-1}). Recrystallization from EtOH gave pure sample: m.p. 111–114°. IR ν_{max}^{KBr} 1737 (shoulder at 1780, C=O) cm^{-1}; NMR ($CDCl_3$) δ 3·85–4·40 (sym. m., 4H, ketal group), 3·35–3·85 (m, 5H), 2·90–3·15 (m, 1H, proton at C_8), 2·07 (s, 3H, Me); (Found: C, 49·64; H, 4·18; Br, 25·68; Calc. for $C_{13}H_{13}BrO_4$: C, 49·86; H, 4·18; Br, 25·52%).

1-*Bromo*-4-*hydroxypentacyclo*[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]*nonan*-9-*one ethylene ketal* (**8**) *from acetate* **7**. A solution of acetate **7** (0·5 g, 1·6 mmole) in dry EtOH (25 ml) containing 0·001 M gaseous HCl, was heated under reflux for 3 hr. The EtOH was removed *in vacuo* at room temp to give crude alcohol **8** (0·4 g, 87%) as a colourless oil which solidified on standing at 20°. The product was almost pure as indicated by IR and GLC. Careful crystallization from cyclohexane furnished an analytically pure sample, m.p. 90–95°, (dec.). IR ν_{max}^{KBr} 3515, 3425, 3235 (OH) cm^{-1}. NMR (C_6D_6) δ 3·35–4·08 (sym.m., 4H, ketal group), 3·15–3·38 (m, 5H), 2·55–2·85 (m, 1H, proton at C_8); *m/e* 271 (M^+, 1 Br). (Found: C, 48·52; H, 4·35. Calc. for $C_{11}H_{11}BrO_3$: C, 48·73; H, 4·09%).

1-*Bromopentacyclo*[4,3,0,0^{2,5},0^{3,8},0^{4,7}]*nonan*-9-*one ethylene ketal* 4-*amino hydrochloride* (**11**). To a stirred ice-cooled solution of acid **1** (7·0 g, 0·024 mole) in acetone (50 ml) and water (4 ml) was added dropwise Et_3N (2·8 g, 0·029 mole) in acetone (50 ml). After addition, a solution of ethyl chloroformate (3·3 g, 0·029 mole) in acetone (11 ml) was added during 45 min, then the mixture stirred for 30 min. at 0° and a solution of NaN_3 (2·3 g, 0·036 mole) in water (8·0 ml) added. After being stirred for 2 hr at 0°, the mixture was poured onto crushed ice and extracted with benzene. The benzene phase was dried ($MgSO_4$), and small part of the solution was concentrated to give the azide **9** as a crystalline solid, IR bands at 2200 (N_3) and 1705 (C=O) cm^{-1}. The dried benzene solution was heated under reflux for 1 hr. and solvent removed *in vacuo* affording isocyanate **10** as an oil, which crystallized on standing. IR $\nu_{N=C=O}$ 2300 cm^{-1}. The crude isocyanate **10** was dissolved in THF (50 ml), conc. HCl (12 ml) was added and the mixture heated under reflux for 1 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 (**11**) (3·5 g, 75%), m.p. 160–180° (lit.[6] 173–180°). IR ν_{max}^{KBr} 3400 (NH_3), 1560 cm^{-1}; NMR (D_2O) δ 3·95–4·35 (m, 4H, ketal group), 3·4–3·9 (m, 5H), 3·0–3·4 (m, 1H, proton at C_8). The crude amine hydrochloride was pure enough for further transformations.

Deamination of **11**. (a) *in water*. A solution of **11** (0·7 g, 2·3 mmole) in 10% AcOH (10 ml) was cooled to 0°. $NaNO_2$ (1·0 g, 14 mmole) was added in small portions during 1 hr. After stirring at room temp for 3 hr the mixture was extracted with ether and the extracts washed with $NaHCO_3$ aq (5%) and water. After drying, the solvent was removed affording alcohol **8** (0·60 g, 93%) as an oil, which solidified on standing at room temp. The spectra are identical with those obtained from the alcohol derived from acetate **7**.

(b) *in acetic acid.* $NaNO_2$ (2·0 g, 0·028 mole) was added in small portions during 2 hr to a solution of **11** (0·5 g, 0·016 mole) in AcOH. After stirring at room temp for 16 hr the solution was neutralized with $NaHCO_3$ aq. The mixture was ether extracted and the ether phase washed with $NaHCO_3$ aq and water. After drying ($MgSO_4$), solvent was removed yielding an oil which crystallized on standing. GLC showed the presence of 3 components. The solid was dissolved in benzene and chromatographed over silica. Elution with benzene furnished the 1-bromo-4-chloropentacyclo[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]nonan-9-one ethylene ketal **13** (0·1 g, 23%). Recrystallization from EtOH gave a pure sample, m.p. 118·5–120 (lit.[6]: 120–123°): IR ν_{max}^{KBr} 3020, 1290, 660 cm^{-1}: NMR ($CDCl_3$) δ 3·80–4·40 (sym.m., 4H, ketal function), 3·55–3·74 (m, 5H), 2·93–3·20 (m, 1H, proton at C_8): *m/e* 254 (M^+–Cl, 1 Br). Correct analysis (C, H, Br, Cl) for $C_{11}H_{10}BrClO_2$. Further elution with $CHCl_3$ yielded a mixture of acetate 7 (47%) and alcohol **8** (4%). The yields were determined by GLC (column: SE 30, $\frac{1}{8}$", temperature 200°).

(c) *in formic acid.* The same procedure as in the deamination of **11** in AcOH was used. Work up gave an oil. GLC showed two components. IR (ν_{OH} 3400, $\nu_{C=O}$ 1710 cm^{-1}) and NMR (HCOO: δ 8·1) indicated a mixture of formate **12** and alcohol **8**. Attempts to separate the two compounds by column chromatography failed. GLC analysis showed formate **12** and alcohol **8** to be present in the ratio 4:3 (yields 42% and 30% respectively).

1-*Bromopentacyclo*[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]*nonane* 4-*carboxylic acid* (**14**). A solution of acid **2**^{3,6} (3·0 g, 0·011 mole) in hydrazine hydrate (60 ml, 100%) was refluxed overnight. After cooling, diethylene glycol (90 ml) and KOH (4·5 g) were added. The apparatus was arranged for distillation and the mixture was slowly heated in an oil bath to 220° and was maintained for 3 hr. The mixture was allowed to cool, poured into water and ether extracted. The water layer was acidified and ether extracted. This ether phase was dried ($MgSO_4$) and concentrated to give crude acid **14**, (2·1 g, 79%). A pure sample was obtained by crystallization from MeOH/water, m.p. 172–173°. IR ν_{max}^{KBr} 3000 (broad OH), 1670 (C=O) cm^{-1}: NMR ($CDCl_3$) δ 3·17–3·85 (m, 6H), 2·15 (d, J = 1·5 Hz, 2H, protons at C_9): *m/e* 241 (M^+, 1 Br). (Found: C, 49·76; H, 3·87; Br, 32·93. Calc. for $C_{10}H_9BrO_2$: C, 49·81; H, 3·76; Br, 33·15%).

1-*Bromopentacyclo*[4.3 0.0$^{2\ 5}$.0^{3,8}.0^{4,7}]*nonane* 4-*amino hydrochloride* (**15**). The same procedure as for the preparation of amine hydrochloride **11** was used. Acid **14** gave a quantitative yield of **15**, m.p. > 250°. Crystallization from AcOEt/MeOH gave an analytically pure sample. IR ν_{max}^{KBr} 3410, 3330, 3220 (NH_3^+) cm^{-1}: NMR (CD_3OD) δ 3·2–3·8 (m, 6H), 2·18 (d, J = 1·5 Hz, 2H, protons at C_9). (Found: C, 43·44; H, 4·39; Br, 32·47; Cl, 13·81; N, 5·57. Calc. for $C_9H_{11}BrClN$: C, 43·48; H, 4·46; Br, 32·14; Cl, 14·26; N, 5·64%).

1-*Bromopentacyclo*[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]*nonane* 4-*acetate* (**16**) *by deamination of* **15**. The same procedure as for the deamination of **11** in AcOH was used. A mixture of chloride **17** and acetate **16** was obtained and separated by chromatography on silica. Elution with hexane afforded the chloride **17**. Further elution with benzene gave the acetate **16** as an oil. Crystallization from hexane at −60° and subsequent sublimation (50°/12 mm) afforded the pure acetate **16** in 50% yield, m.p. 54–56°. IR ν_{max}^{KBr} 1730 (shoulder at 1770, C=O) cm^{-1}: NMR ($CDCl_3$) δ 3·1–3·8 (m, 6H), 2·17 (d, J = 1·5 Hz, 2H, protons at C_9) 2·02 (s, 3H, Me). (Found: C, 51·70; H, 4·49; Br, 31·55. Calc. for $C_{11}H_{11}BrO_2$: C, 51·79; H, 4·35; Br, 31·33%).

1-*Bromo*-4-*hydroxypentacyclo*[4,3,2,0^{2,5},0^{3,8},0^{4,7}]*nonane* (**18**). The same procedure as for the ethanolysis of **7** was used. Acetate **16** gave alcohol **18** as a crystalline solid in almost quantitative yield. IR ν_{max}^{KBr} 3250 (broad OH) cm^{-1}, NMR ($CDCl_3$) 3·0–3·7 (m, 6H), 2·7 (broad singlet, 1H, OH), 2·1 (d, J = 1·5 Hz, 2H, protons at C_9). Treatment of **18** with an ethereal solution of acetylchloride gave acetate **16**.

1-*Bromopentacyclo*[4,2,0,0^{2,5},0^{3,8},0^{4,7}]*octane* 4-*amino hydrochloride* (**23**). The same procedure as for the preparation of amine **11** was used. A 90% yield of crude **23** was obtained from acid **19**. The amine could not be obtained analytically pure; it was characterized by its urethane **22** prepared from isocyanate **21**, m.p. 162–166 (recrystallized from EtOH). IR ν_{max}^{KBr} 3285 (N—H), 1705, 1688 (split C=O) cm^{-1}. NMR ($CDCl_3$) δ 5·0–5·5 (broad absorption, NH), 4·12 (s, 6H), 3·66 (s, 3H, Me). *m/e* 256 (M^+, 1 Br). (Found: C, 47·11; H, 3·97; Br, 30·92; N, 5·44; Calc. for $C_{10}H_{10}BrNO_2$: C, 46·89; H, 3·94; Br, 31·21; N, 5·47%).

1-*Bromo*-4-*hydroxypentacyclo*[4,2,0,0^{2,5},0^{3,8},0^{4,7}]*octane* (**24**). $NaNO_2$ (1·0 g, 0·014 mole) was added in small portions to an ice-cooled solution of amine **23** (0·3 g, 13 mmole) in HCl aq (10 ml, 5%). After stirring for 3 hr the mixture was extracted with ether. The extracts were washed with $NaHCO_3$ aq (5%) and dried ($MgSO_4$). Solvent was evaporated giving alcohol **24** (0·15 g, 60%) as a crystalline solid. Two crystallizations from hexane gave an analytically pure sample, decomposition > 100°. IR ν_{max}^{KBr} 3100 (broad OH) cm^{-1}: NMR ($CDCl_3$): δ 4·05 (s, 6H): 3·15 (s, 1H, OH). (Found: C, 4829; H, 3·67; Br, 39·85; Calc. for C_8H_7BrO: C, 48·27; H, 3·55; Br, 40·14%).

1-*Bromopentacyclo*[4,2,0,0^{2,5},0^{3,8},0^{4,7}]*octane* 4-*acetate* (**25**). The same procedure as for the deamination of **11** in AcOH was used, giving a mixture of acetate **25** and chloride **26** which was separated by chromato-

graphy over silica. Elution with hexane furnished the 1-bromo-4-chloropentacyclo[4,2,0,$0^{2,5}$,$0^{3,8}$,$0^{4,7}$]octane (**26**, 10%). Recrystallization from hexane and subsequent sublimation (100°/12 mm) afforded a pure sample, m.p. 165–167°. IR ν_{max}^{KBr} 1250, 1040, 830 cm^{-1}: NMR ($CDCl_3$) δ 4·20 (s, 6H); *m/e* 102 (M^+—Br, Cl): (Found: C, 44·23; H, 2·89; Br, 36·96; Cl, 15·93. Calc. for C_8H_6BrCl: C, 44·18; H, 2·78; Br, 36·74; Cl, 16·30%). Further elution with benzene gave acetate **25** (50%) as a crystalline solid, m.p. 50–51° (pentane). IR ν_{max}^{KBr} 1735 (C=O) cm^{-1}: NMR ($CDCl_3$) δ 3·95–4·43 (m, 6H), 2·07 (s, 3H, Me). (Found: C, 49·90; H, 3·87; Br, 32·83; Calc. for $C_{10}H_9BrO_2$: C, 49·82; H, 3·76; Br, 33·14%).

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