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SYNTHESIS OF FUNCTIONALIZED BASKETANES BY A REGIOSPECIFIC CAGE EXPANSION OF HOMOCUBANONES†§

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Abstract—The synthesis of 4-substituted basketanes **11** is realized by a regiospecific one carbon-homologation of the readily available 4-substituted homocubanones **10**. Subsequent group transformations, starting from basketanone 4-carboxylic acid **11a**, leads to an efficient synthesis of basketane 4-acetates **16**.

The highly strained basketane skeleton was first synthesized in 1966 independently by Masamune[1] and Dauben.[2] Their syntheses and most of those developed since for derivatives of basketane[3]‡ employ as the key steps (*i*) the Diels–Alder addition of a cyclooctatetraene and a dienophile (e.g. maleic anhydride) and (*ii*) the photochemical ($\pi^2+\pi^2$) intramolecular cyclization of this adduct to the basketane cage structure (Scheme 1).

This approach suffers from serious drawbacks as cyclooctatetraenes are expensive reagents, the photocyclization reaction proceeds only with relatively low yields and the substitution pattern of the cage system is limited. In connection with our continued interest in the chemical reactivity of highly strained bridgehead functionalized cage compounds we needed access to 4-substituted basketanes. This paper deals with a synthetic approach to these compounds which is based on a one-carbon homologation reaction of related cage systems.

As shown previously,[5] cyclopentanone can readily be converted into the 1,5 - dibromo - 1,3 - bishomocubanone **1**. Starting from this compound two routes are conceivable for the preparation of the desired basketanes. Firstly, one carbon cage expansion of the 1,3 - dishomocubanone **1** to the trishomocubane **2** followed by a cage contraction (route A, Scheme 2).

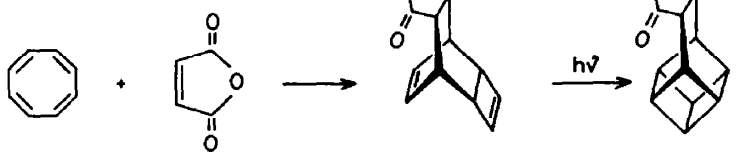
Secondly, by a contraction of **1** to homocubane **3** and a subsequent homologation hereof to the basketane **4** (route B, Scheme 2). The feasibility of this approach using cage expansion reactions is supported by the report of Yonemitsu *et al.*[6] These authors showed that bishomocubanones indeed can be expanded upon reaction with diazomethane. Furthermore, it should be noted that Key[7] suggests that formation of a cage expanded product, although its actual structure was not established, from the reaction of 1,3 - bishomocubanone **1** with CH_2N_2.

Route A. Treatment of 1,3 - bishomocubanone **1** with an excess of ethereal CH_2N_2 produced in a sluggish reaction after 3 days at 0° a precipitate which was crystallized from acetic acid (m.p. 250–260, 25% yield). Although both the mass spectrum (*m/e* 376, M^+) and IR spectrum (C=O, 1720 cm^{-1}) indicated the formation of a single cage expanded product, the ^1H NMR spectrum (CD_3NO_2) was too complex to allow an unequivocal differentiation between structure **5** and its regio-isomer (Scheme 3).

The product obtained was subjected to a Wolff–Kishner reduction in order to remove the ethylene bridge ketone function. Unexpectedly, under the conditions successfully used for the reduction of 1 - bromohomocubanones,[8] ketone **5** produced a complex mixture from which compound **6** was obtained in only 2% yield. Probably, an excessive cage degradation has taken place during the severe reduction conditions. Similar poor results were obtained when the 1 - bromobasketanones **11** (Scheme 4, *vide infra*) were reduced under these Wolff–Kishner conditions. An alternative conversion of **5** to **6** would be the reductive cleavage of the 11 - thioethylene ketal derivative **7** with Raney nickel.

Unfortunately, in all our attempts to prepare this thioketal by treating ketone **5** with dithioglycol and BF_3–Et_2O, a mixture of monothioketal **7** and dithioketal **8** was produced. From the above results it is clear that the prospects for method *A* are rather discouraging. Therefore, this route was abandoned.

Route B. The starting material for this approach is the homocubanone derivative **9a** (Scheme 4) which is readily

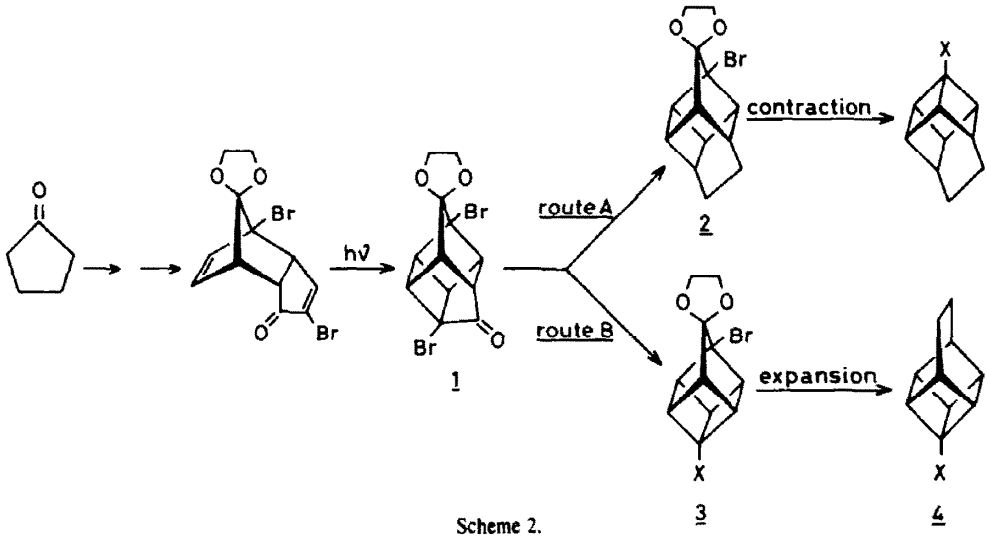


Scheme 1.

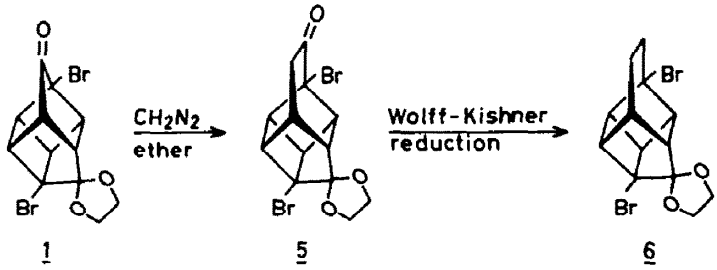
†This work was presented at the Annual Meeting of the Netherlands Foundation for Chemical Research (SON), Lunteren, The Netherlands, October 1977.

‡Shortly, after we completed the work presented in this paper, Gassman *et al.*[4] reported an elegant alternative route to functionalized basketanes which also circumvents the use of cyclooctatetraenes. This route involves a Diels–Alder reaction of cyclohexadiene with 2,5 - dibromobenzoquinone, a photocyclization and a double cage contraction reaction.

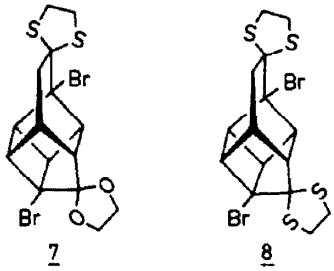
§Dedicated to Prof. Dr. R. J. F. Nivard on the occasion of his 60th birthday.

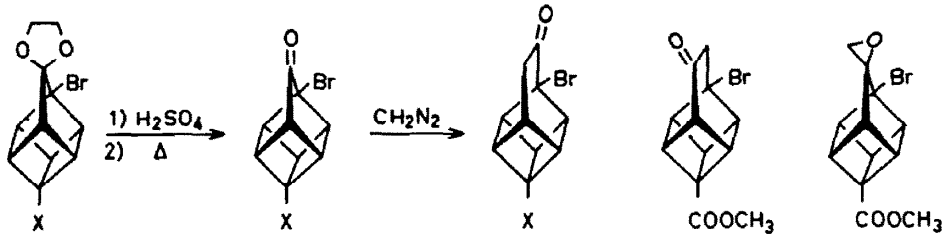


Scheme 2.



Scheme 3.





9a X = COOH
9b X = $COOCH_3$
9c X = Br
9d X = CH_3

10a-d 11a-d 12 13

Scheme 4.

available from cyclopentanone. Hydrolysis of the ketal function and subsequent esterification afforded the hydrate of **10b** which was dehydrated in refluxing toluene. Treatment of ketone **10b** with an excess of ethereal CH_2N_2 for 3 days at 0° led to a mixture of products among which starting material and a cage expanded product dominated. The latter compound could be readily isolated from the mixture in 50% yield by chromatography over silica gel and was identified as basketanone **11b**. The mass spectrum revealed the introduction of a single methylene unit, exhibiting intense peaks at *m/e* 282, 284 (M^+, 1 Br) and *m/e* 240, 242 (loss of ketene). The IR spectrum showed a broad C=O absorption at 1720 cm^{-1}. The ^1H NMR spectrum ($CDCl_3$) displayed a complicated pattern between δ 3.40–3.75(5 H) and δ 3.95–4.15(1 H) for the six bridgehead cage protons, a singlet at δ 3.64(3 H) for the $-OCH_3$ group and a characteristic doublet ($J = 2.5$ Hz) at δ 2.52 ppm for the bridge methylene protons. The latter signal could unambiquously be assigned since in the ^1H NMR spectrum of the product, obtained by treatment of **11b** with NaOMe in MeOD, this absorption was completely absent, while there were no other changes in the remainder of the spectrum. These spectral data exclude homocubyl epoxide **13**, which is conceivable by initial attack of CH_2N_2 at the C_9-carbonyl function of **10b**, and the regio-isomeric basketanone **12** which could have been formed by migration of the C_1–C_9 bond. Careful analysis of the original reaction mixture did not give any indications for the formation of these compounds.

Hence, the cage expansion reaction of 1 - bromohomocubanone **10b** with CH_2N_2 is a regiospecific process which proceeds with exclusive migration of the C_8–C_9 bond. The same regiospecificity was observed for the 4-bromo- and 4-methyl substituted homocubanones **10c** and **10d**, which upon treatment with CH_2N_2 gave the basketanones **11c** and **11d**, resp. in 50–60% yield. Assuming that the mechanism of the ring expansion involves charge separation, the basketanones **11b**, **11c** and **11d** are the expected ones as migration of the more electron rich C_8–C_9 bond in the homocubanones **10b**, **10c** and **10d** should be favored over the migration of the C_1–C_9 bond to the positive CH_2 terminus. The regiospecific reaction shown here also substantiates the formation of **5** from **1** depicted in Scheme 3.

Attempts to enhance the efficiency of the cage expansion reaction by addition of BF_3–Et_2O or MeOH (see Refs. 6 and 9) met with no sucess. Both the reaction rate and the product formation were not affected.

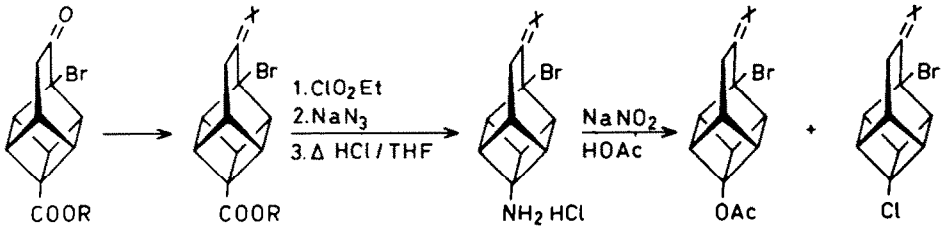
Basketanone **11b** was converted into the corresponding acid **11a** by acid catalyzed hydrolysis. Subsequent ketalization provided the C_{10}-protected ketone acid **14a** in high yield (Scheme 5). The dithioketal analogue **14c** was obtained almost quantitatively from ester **11b** by treatment with dithioglycol/BF_3–Et_2O, followed by base hydrolysis. These carboxylic acids **11a**, **14a** and **14c** are versatile intermediates for the synthesis of 4-functionalized basketanes. The 4-aminobasketanes **15b** and **15c** were prepared in 60–70% yield by conversion of **14c** and **11a** into the corresponding carbonylazides followed by a Curtius rearrangement. When **14a** was subjected to this reaction sequence exclusive formation of aminoketone **15c** was observed. Apparently, under the acidic conditions (HCl aq./THF) applied for the hydrolysis of the intermediate isocyanate, the ethylene ketal function is not stable. This instability is unexpected since in the homocubane series such a facile hydrolysis of the bridge ethylene ketal function has never been observed.[8] The bridgehead acetates **16b** and **16c** could be readily obtained by deamination of **15b** and **15c**, respectively with $NaNO_2$ in AcOH.

A mixture of the acetates **16** and chlorides **17** was produced which could easily be separated by chromatography over silicagel. The acetates are reasonably stable compounds both under neutral and slightly acidic conditions. Basketanone acetate **16c** could even be converted into the ketal and dithioketal derivatives **16a** and **16b** by treatment with glycol and dithioglycol, resp. under acid catalysis. However, efforts to prepare 4-substituted basketane alcohols by careful acid or base catalyzed alcoholysis of the corresponding acetates **16** failed. Instead an interesting cage opening reaction takes place, which will be discussed in the accompanying paper. In conclusion, the results presented in this paper show that the regiospecific one-carbon homologation of homocubanones followed by functional group transformations offers an attractive route for the synthesis of a variety of functionalized basketanes.

EXPERIMENTAL

IR spectra were run on a Perkin-Elmer 257 grating spectrometer. NMR spectra were recorded on a 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 Nijmegen.

1,5 - *Dibromopentacyclo*[5.4.0.$0^{2,6}$.$0^{3,9}$.$0^{5,8}$]*undecan* - 4,11 - *dione* - 4 - *ethylene ketal* **5**. To a soln of ketone **1**[5] (5.0 g, 13 mmole) in ether (75 ml) was added an excess of an ethereal CH_2N_2 soln. The mixture was allowed to stand at 0° for 3 days.



11a R = H; 11b R = CH_3

14a R = H; X = $O(CH_2)_2O$; 14b R = CH_3; X = $S(CH_2)_2S$; 14c R = H; X = $S(CH_2)_2S$

15a X = $O(CH_2)_2O$; 15b X = $S(CH)_2S$; 15c X = O

16a-c

17a-c

Scheme 5.

The precipitate formed, was filtered off and crystallized from acetic acid (1.3 g, 25%), m.p. 250–260°. IR ν_{max}^{KBr} 1720 (C=O) cm^{-1}; NMR (CD_3CN) δ 4.50–4.05 (m, 4H, ketal protons), 4.00–3.00 (m, 5H), 2.85–2.55 (m, 3H); *m/e* 376 (M^+), 297, 295 (M^+–Br), 269, 267 (M^+–[Br + CO]), 215 (M^+–2Br). The filtrate was concentrated to give a complex mixture of products which was not further elaborated.

Wolff–Kishner reduction of **5**. The procedure as described for the reduction of homocubanone **10a** was used.[8] Starting from trishomocubanone **5** (2.3 g, 6 mmole) 1,5 - *dibromopentacyclo*[5.4.0.$0^{2,6}$.$0^{3,9}$.$0^{5,8}$]*undecan* - 4 - *one ethylene ketal* **6** (0.04 g, 2%) was obtained as a crystalline solid, m.p. 125.5–128°. IR ν_{max}^{KBr} 1300, 1120, 1040 cm^{-1}; NMR ($CDCl_3$) δ 4.6–3.8 (m, 4H, ketal protons), 3.8–2.9 (m, 4H), 2.9–2.5 (m, 2H), 2.4–1.6 (m, 4H); *m/e* 362 (M^+), 281, 283 (M^+–Br). (Found: C, 43.41; H, 3.98. Calc. for $C_{13}H_{14}O_2Br_2$: C, 43.1; H, 3.90%).

Methyl pentacyclo[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one* 4 - *carboxylate* **11b**. To a suspension of the hydrate of **9a**[5] (10.0 g, 0.036 mole) was added an ethereal soln of CH_2N_2 (175 ml, 0.058 mole). After stirring at room temp for 1 h, the soln was filtered and the filtrate concentrated to give the hydrate of **10b**. Dehydration was accomplished by refluxing in toluene for ~1 h using a Dean–Stark separator. Removal of the solvent gave crude ketone ester **10b** (8.8 g). To a soln of **10b** in ether (120 ml) was added an excess of an ethereal soln of CH_2N_2. The mixture was allowed to stand at 0° for 3 days. The soln was concentrated to give a mixture of mainly starting ester **10b** and basketone **11b**. Chromatography over silica, elution with $CHCl_3$/toluene (85:15), afforded **11b** (5.0 g, 50%). Recrystallization from hexane gave an analytically pure sample, m.p. 124–126°. IR ν_{max}^{KBr} 1718 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.15–3.95 (m, 1H), 3.75–3.40 (m, 5H), 3.64 (s, 3H, OCH_3), 2.52 (d, J ≃ 2.5 Hz, 2H, $-CH_2-$); *m/e* 284, 282 (M^+, 1Br), 242, 240 (M^+–CH_2=C=O), 161 (M^+–[Br + CH_2CO]). (Found: C, 50.99; H, 3.93; Br, 28.36. Calc. for $C_{12}H_{11}O_3Br$: C, 50.90; H, 3.92; Br, 28.22%).

1,4 - *Dibromopentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one* **11c**. The same procedure as for the cage expansion of **10b** was used. Dibromide **10c**[8] gave a mixture of mainly **11c** and **10c** which was separated by chromatography over silica gel. Elution with toluene furnished dibromide **11c** (45%). Crystallization from hexane gave a pure sample, m.p. 187.5–190°. IR ν_{max}^{KBr} 1711 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.35–4.10 (m, 1H), 4.05–3.70 (m, 2H), 3.75–3.50 (m, 3H), 2.55 (d, J ≃ 2.5 Hz, $-CH_2-$); *m/e* 304 (M^+), 262 (M^+–[CH_2CO]), 183, 181 (M^+–[CH_2CO + Br]), 102 (M^+–[CH_2CO + 2Br]). (Found: C, 38.86; H, 2.78; Br, 51.48. Calc. for $C_{10}H_8OBr_2$: C, 39.51; H, 2.65; Br, 52.57%).

1 - *Bromo* - 4 - *methyl pentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one* **11d**. To a soln of **10d**[8] (3.25 g, 14.5 mmole) in ether (50 ml) was added an excess of an ethereal soln of CH_2N_2. The mixture was allowed to stand at 0° for 5 days. The solvent was removed to give a mixture of starting material **10d** and basketone **11d**. Crystallization from a hexane/chloroform solvent mixture gave a pure product **11d** (1.54 g, 45%), m.p. 143.5–147°. IR ν_{max}^{KBr} 1711 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 3.70–3.45 (m, 3H), 3.30–2.85 (m, 3H), 2.48 (d, J ≃ 2.6 Hz, 2H, $-CH_2-$), 1.17 (s, 3H, CH_3); *m/e* 240, 238 (M^+, 1Br), 198, 196 (M^+–[CH_2CO]). (Found: C, 54.73; H, 4.62; Br, 32.98. Calc. for $C_{11}H_{11}OBr$: C, 55.26; H, 4.64; Br, 33.42%).

1 - *Bromopentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one* 4 - *carboxylic acid* **11a**. A stirred suspension of ester **11b** (12.0 g, 0.042 mole) in 6N HCl (95 ml) was refluxed for 45 min. The reaction mixture was concentrated to dryness to give a quantitative yield of crude carboxylic acid **11a** (11.4 g). Crystallization from water gave a pure sample, m.p. 226–228°. IR ν_{max}^{KBr} 3300, 3000 (broad OH), 1720, 1680 (C=O) cm^{-1}; NMR (D_2O, as Na-salt) δ 3.5–4.1 (m); *m/e* 268, 270 (M^+, 1Br), 226, 228 (M^+–CH_2CO), 147 (M^+–[CH_2CO + Br]).

1 - *Bromopentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one ethylene ketal* 4 - *carboxylic acid* **14a**. A mixture of acid (**11a**) (2.0 g, 7.4 mmole), toluene - p - sulfonic acid, ethylene glycol (1.0 g) and benzene (20 ml) was refluxed until H_2O evolution ceased (Dean–Stark separator). The cooled soln was concentrated to give an oily residue which was treated with a KOH/CH_3OH soln (25%). After stirring for 1 h, MeOH was removed, water added and the resulting mixture acidified (HCl. aq). The precipitate was filtered off, washed with water and dried, to give crude carboxylic acid **14a** (2.3 g, 99%). Sublimation *in vacuo* gave an analytical sample, m.p. 203–204°. IR ν_{max}^{KBr} 3000 (broad OH), 1675 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 9.63–9.13 (broad singlet, 1H, OH), 4.29–3.85 (symm. m, 4H, ketal protons), 3.97–3.72 (m, 1H), 3.60–3.34 (m, 4H), 3.27–3.02 (m, 1H), 2.07 (d, J ≃ 3 Hz, 2H, bridge-CH_2-); *m/e* 314, 312 (M^+, 1Br), 233 (M^+–Br), 147 (M^+–[$C_4H_6O_2$ + Br]), 86 ($C_4H_6O_2^+$). (Found: C, 49.92; H, 4.14. Calc. for $C_{13}H_{13}BrO_4$: C, 49.86; H, 4.18%).

Methyl 1 - *bromopentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one ethylene dithioketal carboxylate* **14b**, was prepared according to the method of Janjatovic[10] from ester **11b**. Thus **11b** (1.8 g, 6.36 mmole) gave the crystalline dithioketal ester **14b** (1.75 g, 75%). Recrystallization from hexane gave a pure sample, m.p. 123–125°. IR ν_{max}^{KBr} 1711 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.00–3.30 (m. 8H, thioketal and cage protons), 3.61 (s, 3H, OCH_3), 3.15–2.85 (m, 2H), 2.72 (d, J ≃ 3 Hz, 2H, $-CH_2-$); *m/e* 358, 360 (M^+, 1Br), 327, 329 (M^+–OCH_3), 279 (M^+–Br). (Found: C, 47.19; H, 4.30; Br, 22.25; S, 17.81. Calc. for $C_{14}H_{15}BrO_2S_2$: C, 46.80; H, 4.21; Br, 22.24; S, 17.85%.

1 - *Bromopentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one ethylene dithioketal* 4 - *carboxylic acid* **14c**. A stirred suspension of ester **14b** (2.63 g, 7.32 mmole) in 20% NaOH aq (30 ml) was refluxed for 2.5 h. The soln was acidified with diluted H_2SO_4, extracted with ether. The ether extracts were dried ($MgSO_4$), filtered and concentrated to give crude acid **14c** (2.27 g, 90%). IR ν_{max}^{KBr} 3000, 1675 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 9.8 (1H, COOH), 3.90–3.27 (m, 10H, cage protons and thioketal protons), 2.73 (d, J ≃ 2.5 Hz, 2H, $-CH_2-$). The crude carboxylic acid was sufficiently pure for further transformations.

1 - *Bromopentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one* 4 - *amino hydrochloride* **15c**. To a stirred ice-cooled soln of acid **11a** (20.0 g, 0.0743 mole) in acetone (250 ml) was added dropwise Et_3N (9.1 g, 0.090 mole) in acetone (50 ml). After the addition, a soln of ethyl chloroformate (10.0 g, 0.092 mole) in acetone (50 ml) was added dropwise, the mixture stirred for 2 h at 0°, followed by the addition of a soln of NaN_3 (5.9 g, 0.090 mole) in water (25 ml). After being stirred for 2 h at 0°, the mixture was poured onto crushed ice and extracted with benzene. The benzene phase was dried ($MgSO_4$), filtered and heated under reflux for 2 h. The solvent was removed *in vacuo* affording the corresponding isocyanate as an oil, which crystallized on standing. IR $\nu_{N=C=O}$ 2310 cm^{-1}. The crude isocyanate was dissolved in THF (200 ml), conc. HCl (50 ml) was added and the mixture refluxed for 1.5 h. 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 **15c** (11.7 g, 57%). IR ν_{max}^{KBr} 1720 (C=O), 1575 cm^{-1}. The crude amine hydrochloride was used for further transformations.

4 - *Acetoxy* - 1 - *bromopentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one* **16c**. $NaNO_2$ (49.0 g, 0.710 mole) was added in small portions during 2 h to a soln of **15c** (13.0 g, 0.0470 mole) in AcOH (300 ml). After stirring at room temp for 16 h most of the AcOH was removed *in vacuo*, the residue dissolved in H_2O and the water layer extracted several times with CH_2Cl_2. The combined CH_2Cl_2 layers were washed with $NaHCO_3$ aq. After drying ($MgSO_4$), solvent was removed, yielding a dark solid material (11.6 g). GLC showed the presence of 2 components (column: SE 30, 1/8 in., temp 180°). This crude product was chromatographed over silica gel. Gradient elution with cyclohexane/ether mixture (the ether content was increased from 25 vol% to 50 vol% ether) furnished 1 - *bromo* - 4 - *chloropentacyclo*[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]*decan* - 10 - *one* **17c** (1.3 g, 11%). Recrystallization from 2-propanol gave a pure sample, m.p. 170–171°. IR ν_{max}^{KBr} 1715 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.22–4.05 (*t, J = 4.5 Hz, 1H*), 3.90–3.64 (m, 2H), 3.68–3.38 (m, 3H), 2.55 (d, J ≃ 2.5 Hz, 2H, bridge $-CH_2-$); *m/e* 262, 260, 258 (M^+, 1Br, 1Cl), 220, 218, 216 (M^+–CH_2CO), 139, 137 (M^+–[Br + CH_2CO]), 102 (M^+–[CH_2CO + Br + Cl]). (Found: C, 46.38; H, 3.17. Calc. for $C_{10}H_8BrClO$: C, 46.28; H, 3.11%). Further elution with cyclohexane/ether yielded acetate **16c** (5.7 g, 43%). Recrystallization from 2-propanol gave an analytically pure sample, m.p. 155–156°. IR ν_{max}^{KBr} 1750 (sh), 1740, 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.34–4.16 (m, 1H), 3.80–3.45 (m, 5H), 2.51 (d,

$J \simeq 2.5$ Hz, 2H, bridge-CH_2-), 2.06 (s, 3H, CH_3); *m/e* 284, 282 (M^+, 1Br), 242, 240 (M^+-CH_2CO), 161 (M^+-[$CH_2CO + Br$]), 158, 156 (M^+-[$CH_2CO + CHCO_2CCH_3$]). (Found: C, 50.70; H, 3.89; Br, 28.45. Calc. for $C_{12}H_{11}BrO_3$: C, 50.90; H, 3.92; Br, 28.29%).

1 - *Bromopentacyclo*[4.4.0.0^{2,5}.0^{3,8}.0^{4,7}]*decan* - 10 - *one ethylene dithioketal* 4 - *aminohydrochloride* **15b**. The same procedure as for the preparation of amine hydrochloride **15c** was used. Carboxylic acid **14c** gave a 70% yield of **15b**. IR ν_{max}^{KBr} 1580–1560 cm^{-1}. This crude material was used for further transformations.

4 - *Acetoxy* - 1 - *bromopentacyclo*[4.4.0.0^{2,5}.0^{3,8}.0^{4,7}]*decan* - 10 - *one ethylene dithioketal* **16b**. The same procedure as for the deamination of **15c** in AcOH was used. A mixture of chloride **17b** and acetate **16b** was obtained which was subsequently separated by chromatography on silica gel.

Elution with benzene afforded the chloride **17b**. Further elution with benzene gave acetate **16b** (50% yield). Crystallization from ethanol afforded a pure sample, m.p. 135–136°. IR ν_{max}^{KBr} 1765 (sh), 1735 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 3.96–3.70 (m, 1H), 3.76–3.12 (m, 8H, dithioketal protons and ring protons), 3.26–2.90 (m, 1H), 2.66 (d, $J \simeq 3$ Hz, 2H, bridge-CH_2-), 1.97 (s, 3H, CH_3); *m/e* 360, 358 (M^+ (very weak), 1Br), 317, 315 (M^+-CH_3CO), 236 (M^+-Br). (Found: C, 46.88; H, 4.21; Br, 22.32; S, 17.89. Calc. for $C_{14}H_{15}Br_2O_2S_2$: C, 46.80; H, 4.21; Br, 22.24; S, 17.85%.) Alternatively, acetate **16b** could also be prepared by thioketalization of **15c** using essentially the same procedure as described for the synthesis of ketal acetate **16a**.

4 - *Acetoxy* - 1 - *bromopentacyclo*[4.4.0.0^{2,5}.0^{3,8}.0^{4,7}]*decan* - 10 - *one ethylene ketal* **16a**. A mixture of acetate **15c** (0.6 g, 2.12 mmole), ethylene glycol (0.6 g, 9.67 mmole) and toluene-*p* sulfonic acid (0.001 g) was refluxed for 5 h. Water was removed by using a Dean–Stark separator. The soln was cooled, washed with 5% NaOH aq. and water. After drying ($MgSO_4$) the solvent was removed to give crystalline ketal **16a** (0.43 g, 62%), which was recrystallized from 2-propanol, m.p. 114–115°. IR ν_{max}^{KBr} 1776 (sh), 1735 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.33–3.92 (m, 5H, ketal and cage protons), 3.72–3.32 (m, 4H), 3.36–3.10 (m, 1H), 2.08 (s, 5H, $-CH_3$ and bridge-CH_2-); *m/e* 328, 326 (M^+, 1Br), 247 (M^+-Br), 205 (M^+-[$Br + CH_2CO$]). (Found: C, 51.30; H, 4.63. Calc. for $C_{14}H_{15}BrO_4$: C, 51.40; H, 4.62%.)

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