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Efficient synthesis of 4-halo-D_3-trishomocubane derivatives

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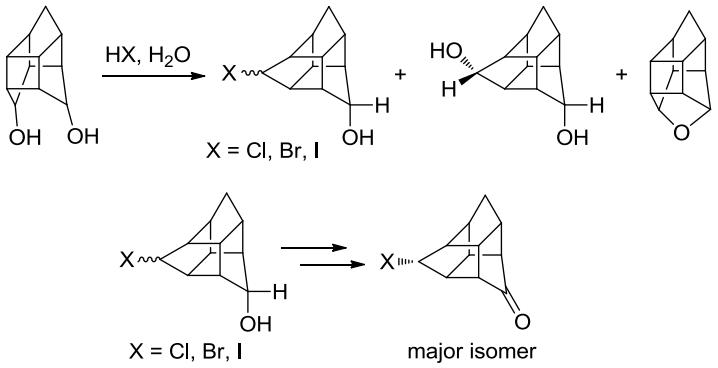
Abstract

Reaction of C_s-trishomocubane-8,11-diol with hydrohalic acids results in haloalcohols – 4,7-disubstituted derivatives of D_3-trishomocubane. The reaction involves the rearrangement of the trishomocubane skeleton and the stereoselective formation of 4,7-D_3-trishomocubanediol and 5-oxahexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{4,8}$.$0^{9,12}$]-dodecane as side products. The mechanism of the rearrangement was proposed. 7-Halo-D_3-trishomocuban-4-ols were oxidized to the corresponding haloketones. The structure of the major isomers of the haloketones was confirmed through X-ray analysis.



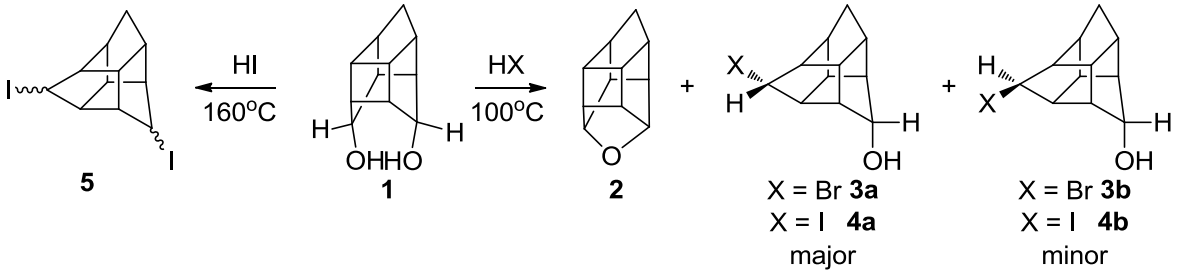
Keywords: C_s-Trishomocubane, D_3-trishomocubane, skeletal rearrangement, haloketone

Introduction

The chemistry of polycyclic cage compounds remains fascinating and continues to draw the attention of organic chemists since the middle of the last century. Interest in the pharmacology of polycyclic cage compounds was stimulated when the wide range of pharmacological properties of adamantane derivatives have been discovered.[1] Since then, plenty of polycyclic hydrocarbon three-dimensional scaffolds were developed. Some of them, like bicyclo[1.1.1]pentane or cubane are considered to be key bioisosteres of traditional flat aromatic systems. [2,3]

D_3-Symmetrical trishomocubane (pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane) has attracted particular attention, because it has specific properties valuable for novel drug design, *viz.*, a relatively large cage size, high lipophilicity, and a conformational rigidity. Actually, around fifty derivatives of D_3-trishomocubane have been tested against 5-HT, adenosine A1, DAT1, dopamine and as NMDA receptors and some of them indeed display pronounced activity.[4-6] Furthermore, unlike the above cages, D_3-trishomocubane is internally chiral, which may also considerably increase the drug efficiency.[7]

However, despite the fact that D_3-trishomocubane derivatives have great potential for drug discovery, their syntheses often remain tricky and the mechanisms of the transformations are still unclear. In particular, rearrangement of C_s-trishomocubane-8,11-diol **1** in acidic media, which is the main method of synthesis of 4,7-disubstituted D_3-trishomocubanes, leads to a mixture of products, and the ratio of them strongly depends on the conditions[8-10]. Thus, the result of the interaction of diol **1** with hydrobromic or hydroiodic acid at 100°C is the formation of a mixture of hexacyclic ether **2** and 7-halo-D_3-trishomocubane-4-ol diastereomers **3a,b** or **4a,b.** At the same time, reaction of C_s-diol **1** with HI under harsh conditions (160°C, 20 h)[8] or of the tosylate of this diol with NaI in HMPA[10] results in a mixture of diastereomers of diiodide **5**, an important compound for the synthesis of homohypostrophene, D_3-trishomocubane, and their derivatives. Another problem is the instability of the yields of 7-iodo-D_3-trishomocubane-4-ols (**4a,b**, Scheme 1), which are varying in a very wide range (from 44% up to 86%) for unclear reasons (stated by Kent[8] and Helmchen[9], confirmed by us[11]).

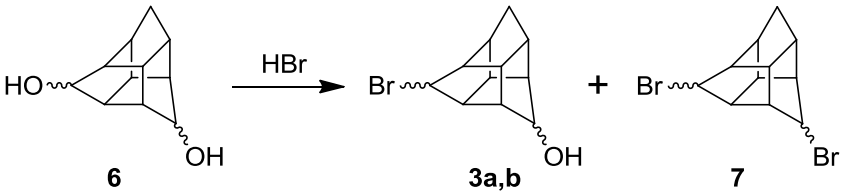


Scheme 1. Reaction of C_s-trishomocubane-8,11-diol (**1**) with HI and HBr.

Note, 7-halo-D_3-trishomocubane-4-ols are starting materials for the synthesis of D_3-trishomocubanone and chiral D_3-trishomocubane-carboxylic acid[11], valuable intermediates for a wide range of D_3-trishomocubane derivatives. Because much in the C_s-trishomocubane-8,11-diol rearrangement under the acidic conditions is still unclear, we decided to reinvestigate this reaction more thoroughly and gain a deeper insight into its mechanism. Optimization of the rearrangement step would increase the overall yield for these compounds, too.

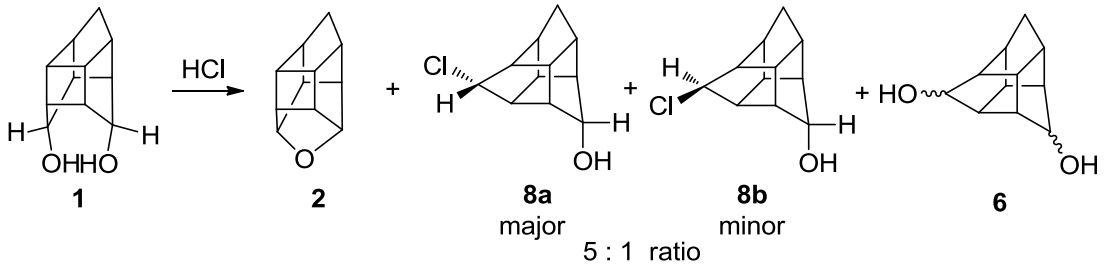
Results and Discussion

First, we carefully investigated the rearrangement of C_s-trishomocubane-8,11-diol **1** in hydroiodic and hydrobromic acids. In our hands, the reaction of **1** with hydroiodic acid gave nearly the same results (with insignificant differences in yields and product ratios) as reported previously.[8,9,11] In the case of aqueous hydrobromic acid, the rearrangement of **1** (Scheme 1) with usual work-up of the reaction mixture (poured into water, extracted by an organic solvent that was then dried and evaporated) results in the mixture of two diastereomeric 7-bromo-D_3-trishomocubane-4-oles **3a,b** in 3:1 ratio (63% yield) with admixture of ether **2** (11% yield). Evaporation of the water layer under normal pressure results in the formation of a chloroform soluble mixture of diastereomeric bromoalcohols **3a,b** and dibromides **7** (approx. 7% yield) (Scheme 2). We suggested that D_3-trishomocubane-4,7-diol **6** can be formed as a by-product of the rearrangement, be well-soluble in aqueous acidic media (unlike C_s-diol **1**, 7-bromo-D_3-trishomocubane-4-oles, and hexacyclic ether **2**) and under heating undergo nucleophilic substitution of the hydroxyl group(s) with bromine. This suggestion can explain the solubility of initially insoluble residue in organic solvent after further boiling in HBr.



Scheme 2. Reaction of D_3-trishomocubane-4,7-diol (**6**) with HBr.

To prove our assumption about the structure of the water-soluble admixture, we attempted the rearrangement of the C_s-diol **1** while boiling in hydrochloric acid (Scheme 3), followed by the treatment as discussed above (extraction with $CHCl_3$, evaporation, e*tc*.). Analysis of the products from the organic phase revealed the presence of the hexacyclic ether **2** and two chloroalcohols **8** in a 5:1 ratio (these diastereomers were separated by crystallization). At the same time, evaporation of the aqueous phase under high vacuum resulted in the formation of a white hygroscopic precipitate. After drying, the precipitate was subjected to NMR and GS/MS analysis and was identified as compound **6**. The yield of 4,7-D_3-trishomocubanediol **6** is *ca.* 20-25%. Difference in ratios of stereoisomers of halo-alcohols (3:1 for **3a,b** and 5:1 for **8a,b**), formed after the reaction of Cs-trishomocubane-8,11-diol with hydrohalic acids, might be explained with different nucleophilicity of the halide anions.



Scheme 3. Reaction of C_s-diol **1** with hydrochloric acid.

Despite the fact that the synthesis of 4,7-D_3-trishomocubanediol **6** was described earlier in a few articles, there is not much physico-chemical data on compound **6** – only IR spectra was reported by Barborak[12]

and later by Naemura.[13] Based on ^{13}C NMR, it was concluded that while compound **6** can exist as three different isomers (one C_1- and two C_2-symmetrical, Figure 1), in the course of the reaction formation of only one, **6a**, takes place.

While structures **6b** and **6c** would have only 6 signals (or 12 in the case of their mixture), in the ^{13}C spectra there are 11 signals, that correspond to structure **6a**.

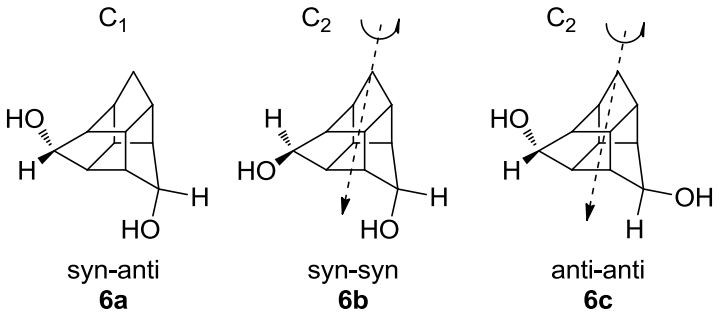


Figure 1. Isomerism and symmetry of 4,7-disubstituted-D_3-trishomocubane with the same substituents.

Also structure of **6a** was proven by X-ray analysis (Figure 2). The hydroxyl groups were shown to have a different orientation in relation to the trishomocubane fragment: the hydroxyl at the C1 atom has an *endo*-position while the hydroxyl group at the C4 atom has an *exo*-position (the O1-C1-C2-C3 and C2-C3-C4-O2 torsion angles are -60.8(1)° and 177.0(1)°).

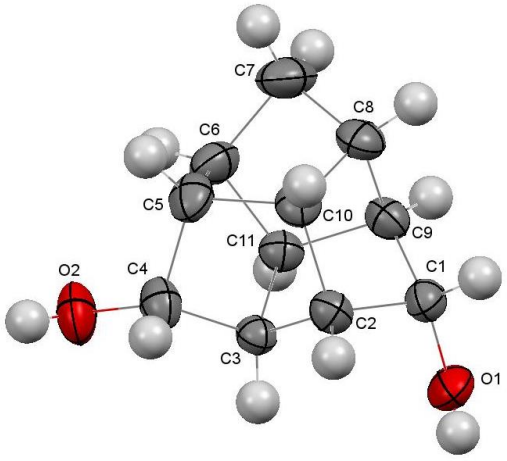
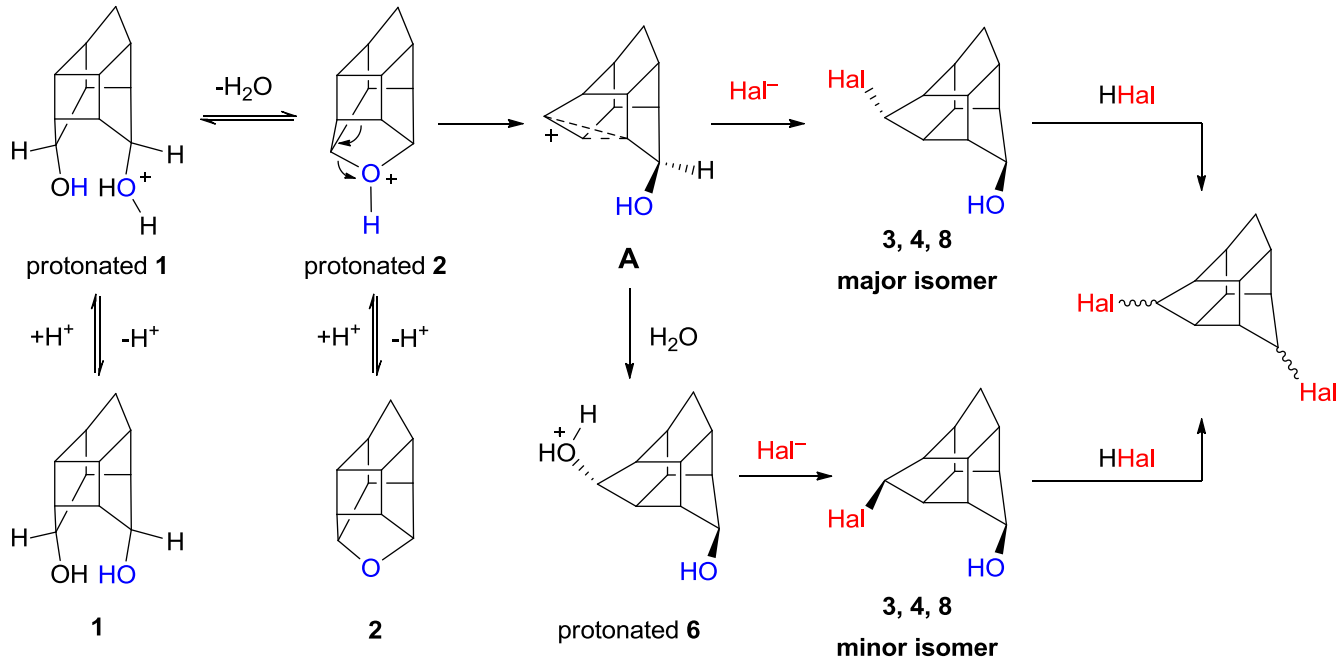


Figure 2. Molecular structure of compound **6a** according to X-ray diffraction data. Thermal ellipsoids are shown at 50% probability level.

It turned out that upon continuous reflux in hydrochloric acid of hexacyclic ether, **2** also undergoes rearrangement to give a mixture of chloroalcohols **8a,b** in approx. 4:1 ratio. However, the reaction proceeds slower than in the case of diol **1**. Treatment of ether **2** with $AlCl_3$ in dichloromethane leads to the same results. Obviously, the mechanism of rearrangement of the C_s-diol **1** in hydrohalic acids suggested earlier by Kent (*via* a concerted halide-displacement/protonation),[8] does not explain the formation of all the observed products. It predicts the formation of only one stereoisomer of 7-halo-D_3-trishomocubane-4-oles while 2 isomers are observed in the mixtures and does envisage the formation of 4,7-D_3-trishomocubanediol **6**. We suggested,

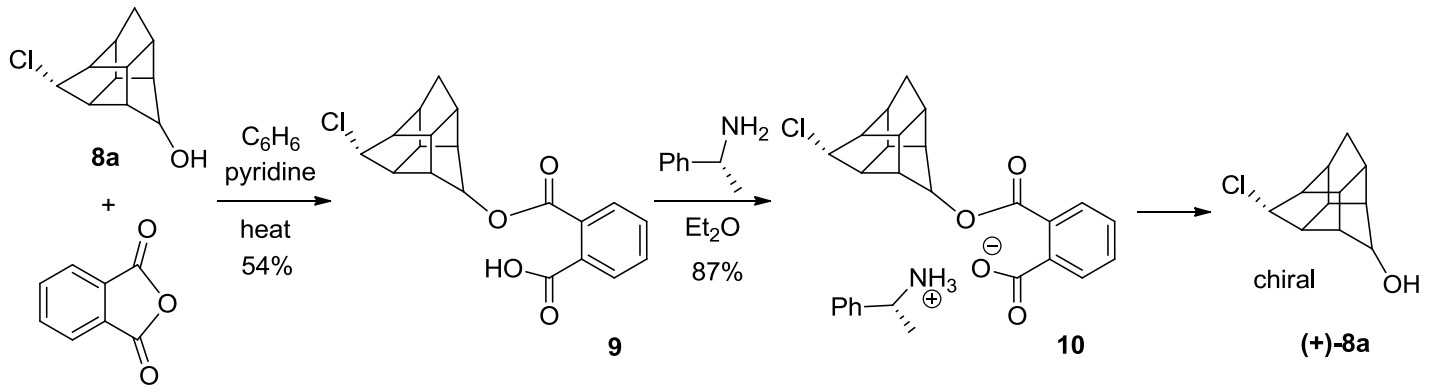
that the mechanism can have additional alternative pathways (Scheme 4), which can be realized via formation of a *nonclassical* $^{+}C^{4}$ D_3-trishomocubane (type **A**). In our previous work[14] we have suggested that a similar rearrangement occurs via the formation of an analogous *nonclassical* cation. We assume that the formation of cation **A** from diol **1** involves protonation of **1**, dehydration, and further rearrangement of the protonated hexacyclic ether **2**. Nucleophilic attack of **A** by a halogen leads to the formation of the major isomer of haloalcohol (**3**, **4**, or **8**). The competing reaction of **A** with water affords protonated diol **6**, where the hydroxyl groups can be further substituted with halogen(s) to furnish the minor isomer of haloalcohol and dihalide.



Scheme 4. Proposed rearrangement pathway.

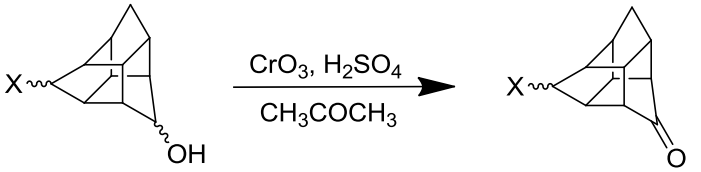
Hydrochloric acid is seen to be the most convenient among the hydrohalic acids for the C_s-trishomocubane-8,11-diol rearrangement because of its high thermal stability and relatively low boiling point. This makes chloroalcohol **8** the most easily accessible haloalcohol and, in advance, the most preferable starting material for further syntheses.

Therefore, we decided to develop the procedure for the chiral resolution of its enantiomers. So, the major isomer of chloroalcohol **8a**, obtained after the fractional crystallization of **8a,b** from acetone, was treated sequentially with phthalic anhydride and (R)-(+)-α-phenylethylamine to obtaine a mixture of diastereomeric esters **10** (Scheme 5). The mixture was separated by fractional crystallization from acetone and the isolated major diastereomer was subjected to basic hydrolysis to furnish the pure enantiomer of 7-chloro-D_3-trishomocubane-4-ol ($[\alpha]_D^{21}$=+69.3(c 1.17, $CHCl_3$) in 35% yield.



Scheme 5. Chiral resolution of 7-chloro-D_3-trishomocubane-4-ol.

7-Halo-D_3-trishomocubane-4-oles **3**, **4**, **8** as well as 4,7-D_3-trishomocubanediol **6** were oxidized with Jones reagent to the corresponding haloketones **11–13** and 4,7-D_3-trishomocubanedione **14** (Scheme 7).



3, X= Br
4, X=I
8, X= Cl
6, X = OH

11 X= Br 78%
12 X= I, 81%
13 X= Cl, 75%
14, X = O, 77%

Scheme 7. Oxidation of haloalcohols **3, 4** and **8** and diol **6** with Jones reagent.

The ratio of the haloketone diastereomers was 2:1 for the chloroketone and 4:1 for the bromo- and iodoketone, the major isomers were isolated from the mixture by crystallization. 2D-NMR of the main diastereomers of the haloketones show an *anti*-orientation of the halogen. Such a structure was confirmed through X-ray analysis of the bromoketone. The bromide substituent has an exo-position in relation to the cubane fragment (the C2-C3-C4-Br1 torsion angle is -179.5(1)°).

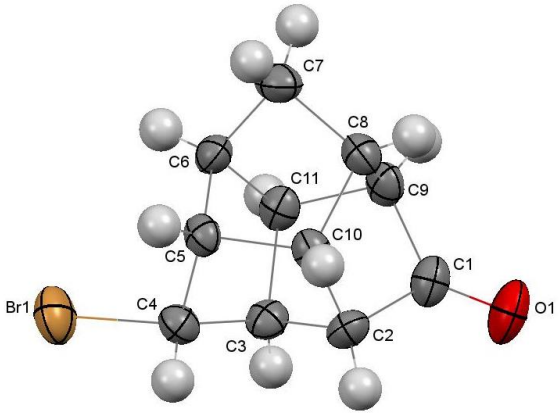


Figure 3. Molecular structure of compound **11** according to X-ray diffraction data. Thermal ellipsoids are shown at 50% probability level.

Conclusions

We have reported a new synthetic pathway leading to the stereoselective formation of 7-halo-D_3-trishomocuban-4-ones and 4,7-D_3-trishomocubanediol. On the basis of the experimental results, a possible reaction mechanism has been proposed. The obtained 7-halo-D_3-trishomocuban-4-ols were oxidized to the corresponding haloketones. The structure of the major isomers of the haloketones was confirmed through X-ray analysis.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded using BrukerAvance NMR spectrometers operating at 400 and 500 ^{1}H frequency (101 and 126 MHz for ^{13}C experiments). Chemical shifts are reported relative to internal TMS (^{1}H) standard. Melting points are uncorrected. Solvents were dried before use according to standard methods. Elemental analysis was carried out in the analytical laboratory of Institute of Organic Chemistry, NAS of Ukraine.

Reaction of C_s-trishomocubane-8,11-diol (1) with hydrobromic acid. A mixture of C_s-trishomocubane-8,11-diol **1** (6.80 g, 38.2 mmol) and 48% aqueous hydrobromic acid (45 mL) was heated to 100°C for 4 h, then cooled to r.t., and poured into water (100 mL). The obtained mixture was extracted with dichloromethane (4 × 50 mL). The combined organic extracts were washed with 3% aqueous NaOH until neutral pH and water (100 mL), dried over Na_2SO_4, and evaporated under reduced pressure to give 7.16 g of crude product, which was subjected to column chromatography (Al_2O_3, hexane, then methanol) to give 5.80 g (yield 63%) of pure 7-bromo-D_3-trishomocubane-4-ol **3a,b** (two diastereomeric pairs of products in approx. 3:1 ratio) and 0.65 g (yield 11%) of 5-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{4,8}.0^{9,12}]dodecane **2**. The aqueous layer was evaporated under reduced pressure to afford 0.70 g (yield 7%) of a mixture of compounds **3** and **7** in approx. 5:1 ratio. Physico-chemical constants of compounds **2**, **3**, and **7** were in agreement with literature data. [8, 15]

Reaction of *C*$_s$-trishomocubane-8,11-diol with hydrochloric acid. A mixture of *C*$_s$-trishomocubane-8,11-diol **1** (5.00 g, 28.1 mmol) and 36% aqueous hydrochloric acid (30 mL) was heated to 100°C for 4 h, then cooled to r.t., and poured into water (50 mL). The obtained mixture was extracted with dichloromethane (4 × 20 mL). The combined organic layers were washed with water (100 mL), dried over Na_2SO_4, and evaporated under reduced pressure to give 3.60 g of crude product, which was subjected to column chromatography (Al_2O_3, hexane, then methanol) to give 0.85 g (yield 19%) of 5-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{4,8}.0^{9,12}]dodecane **2** and 2.00 g (yield 33%) of 7-chloro-*D*$_3$-trishomocubane-4-ol **8a,b** (two diastereomeric pairs of products in approx. 5:1 ratio) as a white solid. It was recrystallized from acetone (3 mL) to obtain 0.82 g of diastereomerically pure 7-chloro-*D*$_3$-rishomocubane-4-ol (**8a**). mp 80°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.20 (1H, br. s.), 4.11 (1H, br. s.), 2.80 - 2.94 (1H, m), 2.66 - 2.79 (1H, m), 2.31 - 2.47 (1H, m), 2.15 - 2.30 (2H, m), 1.93 - 2.13 (4H, m), 1.37, 1.45 (Abq, *J* 10.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ 77.1, 64.0, 53.2, 53.0, 52.4, 49.0, 45.3, 43.6, 41.1, 40.4, 32.9. Anal. Calcd for $C_{11}H_{13}ClO$: C 67.18, H 6.66. Found: C 67.20, H 6.67.

The acidic aqueous solution was evaporated to dryness under reduced pressure and the obtained viscous oil was triturated with acetone and collected by filtration to obtain 1.40 g (yield 28%) of *D*$_3$-trishomocubane-4,7-diol **6** as white crystals. mp 203-205°C.[3] ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ 4.53 (2H, br. s), 3.90 (2H, s), 2.60 (1H, s), 2.28 (1H, br. s), 2.01 - 2.17 (2H, m), 1.77 - 1.91 (4H, m), 1.32, 1.20 (Abq, *J* 9.8 Hz, 2H). ^{13}C NMR (DMSO-*d*$_6$, 126 MHz): δ 75.8, 75.7, 53.2, 51.9, 50.7, 47.7, 44.2, 42.7, 40.6, 39.9, 33.5. Anal. Calcd for $C_{11}H_{14}O_2$: C 74.13, H 7.92. Found: C 74.16, H 7.90.

Chiral resolution of 7-chloro-*D*$_3$-trishomocubane-4-ol. A mixture of 7-chloro-*D*$_3$-trishomocubane-4-ol **8a** (pure diastereomer) (2.85 g, 13.4 mmol), phthalic anhydride (1.08 g, 7.29 mmol), benzene (60 mL), and pyridine (3 mL) was refluxed for 12 h, cooled to r.t., washed with 3% aqueous citric acid (50 mL), and extracted with 10% aqueous Na_2CO_3 (3 × 30 mL). The basic aqueous extract was acidified with 5% hydrochloric acid and extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, and evaporated under reduced pressure to obtain 2.50 g (yield 54%) of 7-chloro-*D*$_3$-trishomocubane-4-ol hydrogen phthalate **9**. The phthalate **9** (2.30 g, 6.67 mmol) was dissolved in diethyl ether (30 mL) and treated with a solution of (*R*)-α-phenylethylamine (0.900 g, 7.43 mmol) in diethyl ether (10 mL) at r.t. The precipitated solid was collected by filtration, washed with diethyl ether, and dried to obtain 2.70 g (yield 87%) of 7-chloro-*D*$_3$-trishomocubane-4-ol phenylethylammonium hydrogen phthalate **10** (mixture of two diastereomers) as a white solid. Its fractional crystallization from acetone afforded 0.60 g (yield 44%) of diastereomerically pure salt **10**. The latter was dissolved in 80% aqueous ethanol (5 mL) and treated with NaOH (0.052 g, 1.29 mmol). The mixture was refluxed for 4 h and then concentrated *in vacuo*. The residue was mixed with water (15 mL) and extracted with diethyl ether (4 × 20 mL). The combined organic layers were washed with 5% hydrochloric acid (3 × 10 mL), dried over Na_2SO_4, and evaporated to give 0.20 g (yield 80%) enantiomerically pure chloroalcohol (+)-**8a**, mp 118°C. $[\alpha]_D^{21}$=+69.3(c 1.17, $CHCl_3$)

***D*$_3$-Trishomocubane-4,7-dione (14).** To a stirred solution of *D*$_3$-trishomocubane-4,7-diol **6** (1.00 g, 5.61 mmol) in acetone (30 mL) Jones reagent (a mixture of CrO_3 (1.00 g, 10.0 mmol), H_2SO_4 (1.7 mL, 31.9 mmol), and water (2.1 mL)) was added dropwise and the reaction mixture was stirred for 1 h at r.t. Then it was poured into water and extracted with dichloromethane (3 × 15 mL). The combined organic layers were washed with water (20 mL), dried over Na_2SO_4, and evaporated under reduced pressure to obtain 0.75 g (yield 77%) of *D*$_3$-trishomocubane-4,7-dione **14**. Physico-chemical constants of compound **14** were in agreement with literature data[12] mp 212°C-213°C (lit. 213°C-214°C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.73 - 2.90 (4H, m), 2.17 - 2.27 (2H, m), 2.05 - 2.16 (2H, m), 1.77 (2H, s). ^{13}C NMR (DMSO-*d*$_6$, 126 MHz): δ 213.3, 54.6, 53.1, 50.1, 48.4, 47.6, 47.1, 42.2, 40.2, 40.1, 34.6. Anal. Calcd for $C_{11}H_{10}O_2$: C 75.84, H 5.79. Found: C 75.80, H 5.81.

General procedure for the preparation of 7-halo-D_3-trishomocubane-4-ones. To a cooled to 0°C solution of 7-halo-D_3-trishomocubane-4-ol (15.0 mmol) in acetone (40 mL) Jones reagent (a mixture of CrO_3 (2.70 g, 27.0 mmol), H_2SO_4 (2.9 mL, 54.4 mmol), and water (5.1 mL)) was added dropwise maintaining temperature below 10°C and the reaction mixture was stirred for 30 min at 10°C and for 12 h at r.t. Then it was poured into water (50 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to obtain the crude product, which was purified by column chromatography (Al_2O_3, hexane/ethyl acetate 9:1) to obtain the appropriate 7-halo-D_3-trishomocubane-4-one as a mixture of two diastereomers. Further recrystallization from hexane ethyl acetate mixture afforded a single diastereomer of the halo-ketone.

7-Bromopentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4-one (11). Obtained in 78% yield as 4:1 mixture of isomers. Recrystallization (hexane/ethyl acetate 3:2) gave 33% yield of diastereomerically pure **11**; mp 90-91°C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.06 (1H, br. s.), 3.17 (1H, br. s.), 2.57 - 2.72 (3H, m), 2.50 - 2.57 (1H, m), 2.38 - 2.49 (1H, m), 1.83 - 2.00 (2H, m),1.68, 1.52 (Abq, *J* 10.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ 213.3, 54.6, 53.1, 50.1, 48.4, 47.6, 47.1, 42.2, 40.2, 40.1, 34.6. Anal. Calcd for $C_{11}H_{11}BrO$: C 55.25, H 4.64. Found: C 55.29, H 4.62.

7-Iodopentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4-one (12). Obtained in 81% yield as 4:1 mixture of isomers. Recrystallization (hexane/ethyl acetate 4:1) gave 31% yield of diastereomerically pure **12**. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.90 (1H, s), 3.26 (1H, br. s), 2.84 (1H, br. s), 2.67 - 2.73 (1H, m), 2.54 - 2.62 (2H, m), 2.43 (1H, q, *J* 5.6 Hz), 1.86 - 1.98 (2H, m), 1.72, 1.50 (Abq, *J* 10.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ 213.1, 54.2, 50.4, 50.0, 49.1, 48.9, 42.9, 40.4, 39.5, 34.4, 30.5. Anal. Calcd for $C_{11}H_{11}IO$: C 46.18, H 3.88. Found: C 46.21, H 3.85.

7-Chloropentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4-one (13). Obtained in 75% yield as 2:1 mixture of isomers. Recrystallization (hexane/ethyl acetate 3:7) gave 25% yield of diastereomerically pure **13**; mp 85°C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.08 (1H, s), 3.11 (1H, br. s.), 2.63 (1H, q, *J* 5.4 Hz), 2.52 - 2.60 (2H, br. d, *J* 12.5 Hz), 2.40 - 2.52 (2H, m), 1.87 - 1.99 (2H, m), 1.69, 1.56 (Abq, *J* 10.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ 213.6, 63.8, 52.9, 49.8, 47.8, 46.9, 46.0, 41.8, 40.0 (overlapped), 34.8. Anal. Calcd for $C_{11}H_{11}ClO$: C 67.87, H 5.70. Found: C 67.90, H 5.68.

X-ray crystallography. The crystals of **6a** ($C_{11}H_{14}O_2$) are monoclinic. At 293 K a = 24.316(4), b = 7.5252(9), c = 10.432(2) Å, β = 114.51(2)°, V = 1736.9(5) Å^3, Mr = 178.22, Z = 8, space group C2/c, d_{calc} = 1.363 g/cm^3, μ(MoK α) = 0.092 mm^{-1}, F(000) = 768. Intensities of 6794 reflections (2533 independent, R_{int} = 0.030) were measured on the "Xcalibur-3" diffractometer (graphite monochromated MoK$_\alpha$ radiation, CCD detector, ω-scaning, 2Θ$_{max}$ = 60°).

The crystals of **11** ($C_{11}H_{11}OBr$) are monoclinic. At 293 K a = 6.364(1), b = 20.331(5), c = 7.030(1) Å, β = 95.42(2)°, V = 905.5(3) Å^3, Mr = 239.11, Z = 4, space group P2$_1$/c, d_{calc}= 1.754 g/cm^3, μ(MoKα) = 4.491 mm^{-1}, F(000) = 480. Intensities of 6805 reflections (2624 independent, R_{int} = 0.050) were measured on the«Xcalibur-3» diffractometer (graphite monochromated MoK$_\alpha$ radiation, CCD detector, ω-scaning, 2Θ$_{max}$ = 60°).

The structures were solved by direct method using SHELXTL package [16]. The absorption correction for **11** was performed using the multi-scan method (T_{min} = 0.346, T_{max} = 0.467). Position of the hydrogen atoms were located from electron density difference maps and refined by "riding" model with U_{iso} = nU_{eq} of the carrier atom (n = 1.5 for methyl groups and n = 1.2 for other hydrogen atoms) in structure **6a** and using isotropic approximation in structure **11**. Full-matrix least-squares refinement of the structures against F^2 in anisotropic approximation for non-hydrogen atoms using 2479 (**6a**), 2595 (**11**) reflections was converged to: wR_2 = 0.144 (R_1 = 0.053 for 1763 reflections with F>4σ(F), S = 1.014) for structure **6a** and wR_2 = 0.072 (R_1 = 0.037 for 1839 reflections with F>4σ(F), S = 0.902) for structure **11**. The final atomic coordinates, and crystallographic data for molecules **6a** and **11** have been deposited to with the Cambridge Crystallographic Data Centre, 12 Union Road,

CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) and are available on request quoting the deposition numbers CCDC 1870778 for **6a** and CCDC 1870777 for **11**).

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