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HYDROGENOLYSIS OF CUBANE[1]

REINHARD STOBER and HANS MUSSO
Institut für Organische Chemie der Universität Karlsruhe, Richard-Willstätter-Allee 2, D-7500 Karlsruhe, F.R.G.

and

EIJI ŌSAWA
Department of Chemistry, Faculty of Sciences, Hokkaido University, Sapporo 060, Japan

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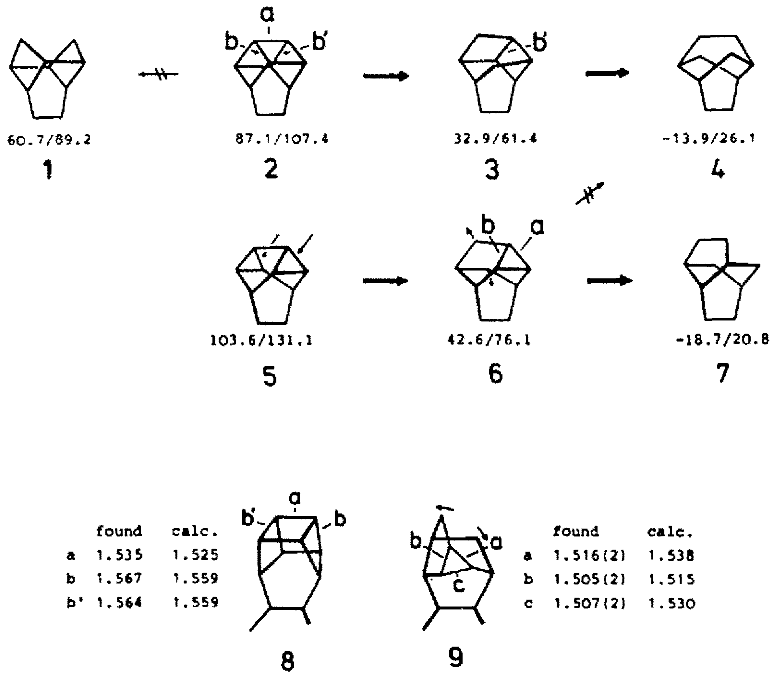
Abstract—On catalytic hydrogenation over Pd–C under normal conditions cubane (**10**) takes up 3 mol of hydrogen in a few hours. Bicyclo[2.2.2]octane (**13**) is formed as the main product, and tetracyclo[4.2.0.0^{2,5}.0^{3,8}]octane (**11**, secocubane) and tricyclo[4.2.0.0^{2,5}]octane (**12**, nortwistbrendane) have been identified as intermediates. The hydrogenolysis of dimethyl 1,4-cubane dicarboxylate, as well as cuneane derivatives, have also been studied. Results are discussed in terms of strain relief calculated by the molecular mechanics method for cubane-like structures.

It has been shown that basketane **2** and some of its derivatives are hydrogenolized under normal conditions of catalytic hydrogenation first at bond b to give the dihydro compound **3** and further at bond b′ to yield twistane **4** as the only product.[2] No trace of a compound of type **1** resulting from hydrogenolysis of symmetrical bond a could be detected despite careful analysis.[3] Under these conditions up to 10% of the basketane derivatives **2** are rearranged into snoutane derivatives **5** and consequently the dihydro product **6** and isotwistane **7** have been isolated. When **5** was separately hydrogenated under the same conditions **6** and **7** were detected, but no twistane **4**. It is remarkable to note that in the case of basketane **2** the bonds b and b′ on opposite sides are cleaved in contrast to snoutane **5** wherein the two bonds are opened from the same side of the molecule. It is well known from the X-ray structure analysis of dimethyl basketane dicarboxylate **8**[4] and the same derivative of dihydrosnoutane **9**[5] that the bond which is opened first is the longest and perhaps the most prestressed one in the 4- or 3-membered rings of the molecule. In this context cubane **10** was hydrogenated since the very high strain energy of that skeleton[6,7] would suggest that three C—C bonds could be hydrogenolyzed without pressure[8,9] at room temperature. In methanol at 20° over Pd–C cubane **10** takes up the first mole of hydrogen in *ca* 2 h and secocubane **11** is formed in high yield. The structure of **11** is not so unusual; nevertheless, it was proven by independent synthesis. Homocubanone **21** was opened with potassium t-butoxide in THF–H$_2$O to the *exo*–*endo* mixture of the carboxylic acids **22**,[10] followed by Grob degradation[11] to the *exo*-chloride **23** and dehalogenation. Comparison of this degradation



	found	calc.
a	1.535	1.525
b	1.567	1.559
b′	1.564	1.559

	found	calc.
a	1.516(2)	1.538
b	1.505(2)	1.515
c	1.507(2)	1.530

Scheme 1.

product and that isolated by preparative VPC from the hydrogenation mixture showed them to be identical.

In secocubane **11** there are four different kinds of cyclobutane bonds a–d, as shown. On further hydrogenation **11** was transformed into a tetrahydro derivative of structure **12** (nortwistbrendane) which is slowly hydrogenated to the final product bicyclo[2.2.2]octane **13**. Both compounds were identified by comparing spectra and VPC retention time with authentic samples. That of **12** was kindly supplied by Askani and Schwertfeger[12] just on time. None of compounds **14**–**16** could be detected.

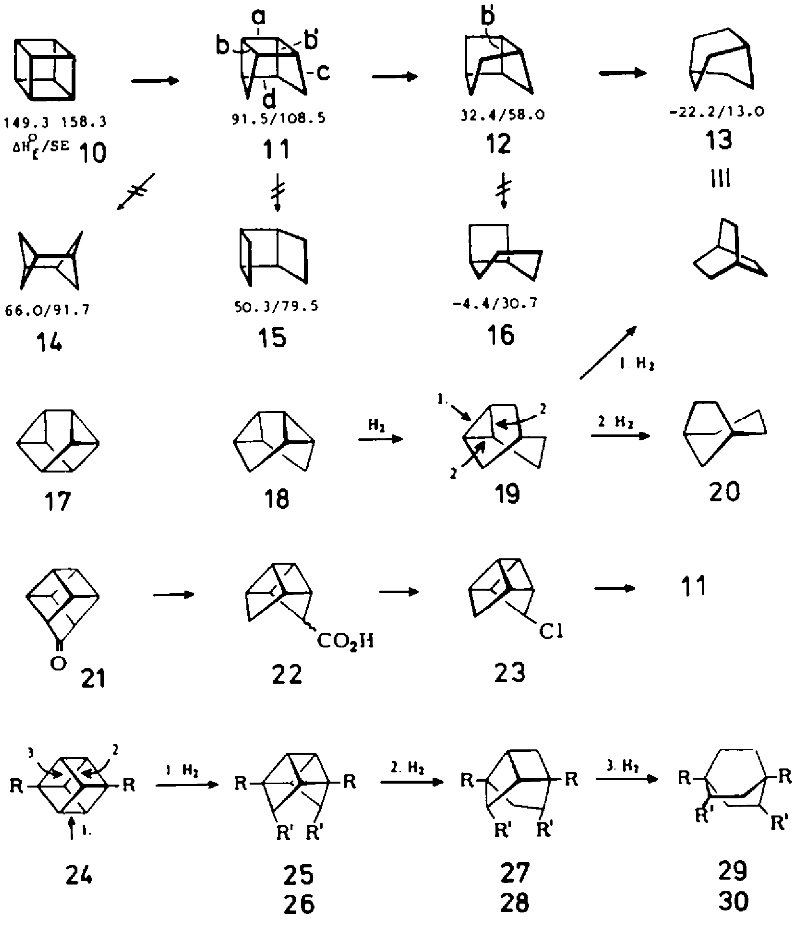
In the final reaction mixture, besides **13** *ca* 12% of an isomeric hydrocarbon was present which was found to be bicyclo[3.2.1]octane **20**, whose formation can be explained in terms of the rearrangement of cubane **10** to cuneane **17**, as well as of secocubane **11** to dihydrocuneane **18** on the catalyst and their subsequent hydrogenations which are already known to yield the bicyclooctanes **13** and **20** via the tricyclooctane **19**.[13] The separate hydrogenation of pure **11** leads via at least three intermediates recognizable by VPC to **13** and **20** in the ratio 4:3.

Hydrogenation of dimethyl cubane-1,4-dicarboxylate **24** over Pd–C in methanol was found to proceed without rearrangement. Pure dimethyl bicyclo[2.2.2]octane-1,4-dicarboxylate **29** was obtained via the dihydroester **25** and the tetrahydroester **27**.[14] The 2,5-diester **30** could be isolated when the *endo,endo*-secocubane-1,4-dicarboxylic acid dimethyl ester **26** was submitted to hydrogenolysis. From these experiments it can be concluded that the diester **24** is attacked specifically at a non-substituted C—C bond and that in the seco derivatives **25** and **26**, like in secocubane **11**, bonds 2 and 3 inclined opposite to the already open bond 1 and common to two 4-membered rings are cleaved.

With Pt in glacial acetic acid hydrogenation of **24** yields mainly **29** but with small amounts of **30**. Compounds **29** and **30** have been identified by comparison with authentic samples.[15,16]

These results provide clear evidence that in secocubane **11** bond opening by hydrogenolysis occurs in the same way as in basketane **2**. Bond a is not broken but bonds b and b′ are.

The reason for this becomes evident on inspection of Table 1 in which the enthalpies of formation (ΔH_f°) and strain energies (*SE*) of the compounds are given by each formula as calculated by molecular mechanics methods.[17] Thus, the formation of secocubane **11** from cubane **10** is favoured by an enormous reduction in *SE* of 54 kcal mol^{-1}, the next step to **12** relieves slightly less



: R = CO_2CH_3, R′ = H
: R = H, R′ = CO_2CH_3

Scheme 2.

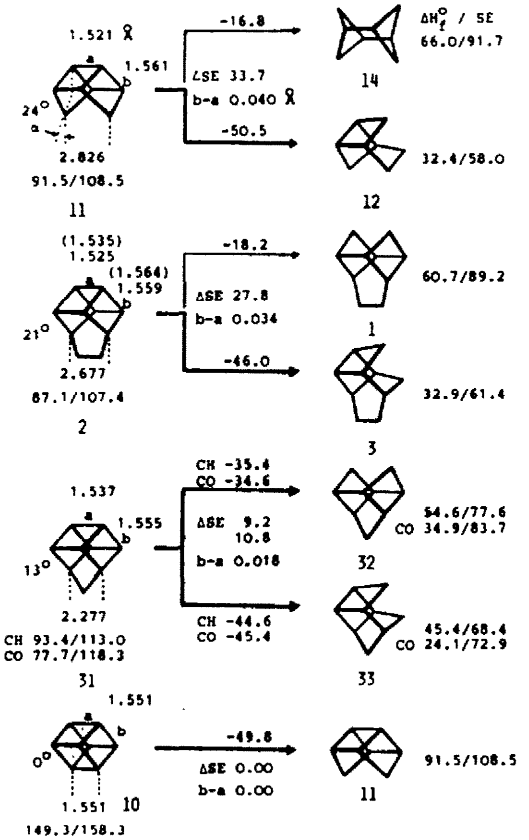
with 50 kcal mol^{-1} and the final step to **13**, 49 kcal mol^{-1}. The formation of the other compounds, those not observed (**14**–**16**), would be much less effective with respect to strain relief. The formation of **14** would liberate 32 kcal mol^{-1} less and that of **15** and **16** *ca* 18 kcal mol^{-1} less than the formation of the isolated products **12** and **13**.

These kind of calculations are not meant to imply that hydrogenations are thermodynamically controlled processes. No isomerization of the final products has been observed on the catalyst. The rearrangement of basketane **2** and cubane **10** to the isomers of lower strain energy snoutane **5**[18] and cuneane **14**[19] is a well-established process in the presence of silver ion.[20] The possibility of a trace of silver in the Pd catalyst being responsible for the partial rearrangements, cannot be excluded, because a Pd or Pt catalyst completely free of Ag was not available.

DISCUSSION

Table 1 gives structural parameters and energy values for secocubane-like structures calculated by force field methods.[17] In secocubane **11** the distance between the seco-carbon atoms C-4 and C-7 is 2.826 Å. The difference in length of bonds b and a is 0.040 Å. The difference in strain energy, *SE*, between the two products **14** and **12** possible by hydrogenolysis of bond b or of bond a is 33.7 kcal mol^{-1}. It is an interesting question as to how these parameters are changed with the carbon atoms C-4 and C-7 are pulled mechanically together as in basketane **2** with a distance of 2.677 Å and homocubane **31** with a distance of 2.277 Å. The difference in bond length, b—a, goes down to 0.034 and 0.018 Å, respectively; the strain relief for the two pathways for hydrogenolysis comes closer to 27.8 (**1** and **3**) and 9.2 kcal mol^{-1} (**32** and **33**). Finally in cubane **11** the C-4—C-7 distance as well as bonds a and b are equal in length. It is evident from these data that the mechanical strain used for bringing the carbon atoms C-4 and C-7 in secocubane **11** closer together is transposed mainly into lengthening bond a from 1.521 to 1.551 Å, whereby bonds b are shortened slightly (0.01 Å).

Table 1. Bond length and strain energies in starting materials and hydrogenolysis products



In the cases of secocubane **11** and basketane **2**, the less strained products **12** and **3** are formed specifically. In the case of homocubane Δ*SE* is much smaller (*ca* 10 kcal mol^{-1}) and both products are formed; hydrogenolysis of bond a is observed to the extent of 20–40% depending on the particular derivative and the catalyst.[21,22]

There are other examples in the literature[17] of Δ*SE* less than 10 kcal mol^{-1} in which hydrogenation gives one single product out of two or more possibilities only and other ones of unsignificant selectivity. For an explanation of the results one should look on the bond length in the starting material and the relief of strain, obtainable from experimental methods or theoretical calculations in high precision and reliability.[23]

Calculations have been carried out at the Rechenzentrum of Universität Karlsruhe, and at the Computing Centers of Hokkaido University and the Institute for Molecular Science. The empirical force field program was kindly donated by Professor P. v. R. Schleyer. The energy data in Table 1 should be correct to within 1–2 kcal mol^{-1}, and the bond distances to within 0.01 Å.[17] The experimental structural data available for **8**–**10** are in reasonable agreement with the calculated ones. The errors should be less than those specified above for the differences (Δ*SE* and b—a) between similar structures where some of the errors inherent to the force field should cancel.

EXPERIMENTAL

General. M.ps uncorrected: Kofler hot-plate microscope, easily sublimable compounds in sealed capillaries. Spectra, IR: Perkin–Elmer 221 and Beckman IR-8; NMR in $CDCl_3$ Bruker WH 90, TMS internal standard; MS: Varian MAT CH-5. Analytical VPC Perkin–Elmer F-6 and 900; preparative scale VPC on Wilkins Autoprep A 700. TLC DC Mikrokarten SI-F Riedel de Haen AG, LC on Silica 0.063 mm Merck. Solutions were dried with $MgSO_4$; solvents were removed *in vacuo* using a rotary evaporator; in the cases of very volatile compounds solvent was removed by distillation through a 15 cm column filled with glass turnings.

Catalysts. Palladium 10% on charcoal (Merck) and PtO_2 (Degussa).

Pentacyclo[$4.2.0.0^{2,5}.0^{3,8}.0^{4,7}$]*octane - 1,4 - dicarboxylic acid* (*cubane-1,4-dicarboxylic acid*). This was prepared according to lit.[24,25] in 43 and 60% yield: m.p. 223–226° (lit. 226° (dec.),[24] 223–224°[25]). The dimethylester (**24**) was obtained in 80% yield on reaction with diazomethane: m.p. 159–160° (lit. 161–162°[6]).

Pentacyclo[$4.2.0.0^{2,5}.0^{3,8}.0^{4,7}$]octane (cubane **10**) was obtained via the 1,4-dibromide[25] and dehalogenation with tri-n-butyl tin hydride[26] in 41% yield; m.p. 125–126° (lit. 124–125°,[25] 130–135°[6]).

Pentacyclo[$3.3.0.0^{2,4}.0^{3,7}.0^{6,8}$]octane - 2,6 - dicarboxylic acid dimethylester (cunean-2,6-dicarboxylic acid dimethylester) and pentacyclo[3.3.0.0^{2,4}.0^{3,7}.0^{6,8}]octane (cuneane **17**) were isolated from the Ag^+ catalyzed rearrangements[19] of the corresponding cubane derivatives in 43 and 95% yield.

endo- and *exo* - Tetracyclo[4.2.0.0^{2,5}.0^{3,8}]octane - 4 - carboxylic acids (secocubane acids **22**) were isolated as a mixture from homocubanone (**21**) in 59% yield following lit.[10]

exo - 4 - *Chlorotetracyclo*[4.2.0.0^{2,5}.0^{3,8}]*octane* (exo - 4 - chlorosecocubane, **23**). Lead tetraacetate (429 mg, 0.92 mmol) was added to the deaerated soln under N_2 of 150 mg of **22** (1.0 mmol) and 773 mg of N-chlorosuccinimide (5.75 mmol) in 15 ml DMF–glacial AcOH (1:1). When the stirred mixture was gently warmed up to 55–60° evolution of CO_2 and disappearance of the yellowish colour occurred within 5 min. After this the soln was extracted at 0° with n-pentane (5 × 20 ml). The combined extracts were washed with perchloric acid (20%) and K_2CO_3 aq (10%), dried and concentrated. Analytical VPC showed three components in 8, 14 and 78% yield (QF 1, 60°). The main product was isolated by preparative VPC (QF 1, 130°) yielding 61 mg (43%) of **23** as a colourless liquid.

(Found: C, 68.22; H, 6.31; Cl, 25.23. C_8H_9Cl (140.2) requires: C, 68.34; H, 6.45; Cl, 25.21.) MS: M^+ 140, *m/e* (2); NMR (δ ppm): 2.28 (m, *exo*-H-7), 2.46 (d, *endo*-H-7, J = 10 Hz), 3.30 (m, 5H), 3.65 (m, H-2), 5.00 (d, *endo*-H-4, J = 2 Hz).

Tetracyclo[4.2.0.0^{2,5}.0^{3,8}]*octane* (secocubane **11**). (a) 6.0 g of small pieces of Na and 60 ml of EtOH in portions were added to a boiling soln of 3.00 g (2.14 mmol) of **23** in 45 ml EtOH within 1 h. After cooling, the turbid mixture was diluted with 350 ml n-pentane and water. From the washed, dried and concentrated pentane soln 107 mg (43%) **11** could be isolated by preparative VPC (OV 17, 90°) as colourless crystals with m.p. 101–103°. (Found: C, 90.25; H, 9.75. C_8H_{10} (106.2) requires: C, 90.51; H, 9.49.) MS: M^+ 106 (7); ^{1}H-NMR: 2.15 (m, 2H, *exo*-H-4,7), 2.43 (d, 2H, *endo*-H-4, 7, J = 10 Hz), 3.04 (qi, 4H, H-3, 5, 6, 8), 3.29 (qi, 2H, H-1, 2, J = 3 Hz). ^{13}C-NMR: 25.9 (C-4, 7), 40.1 (C-3, 5, 6, 8), 47.2 (C-1,2); IR: 2965 (2940 sh), 2860 (1460 sh), 1450, 1290, 1255, 1249, 1225, 1210, 1135, 1010 cm^{-1}.

(b) Dehalogenation with tri-n-butyl tin hydride under illumination and isolation by VPC yielded 13% only.

endo, endo - *Tetracyclo*[4.2.0.0^{2,5}.0^{3,8}]*octane* - 4,7 - *dicarboxylic acid*. This was prepared in 84% yield by oxidation of basketane-9,10-dione according to the lit.[18] Ozonization of basketane and oxidative workup in our laboratory was less successful (21%), m.p. 238–240 (dec.) (lit. 240–242° [18]). *endo,endo*-**26** was obtained from the acid with ethereal diazomethane after chromatography on silica as colourless crystals in 83% yield, m.p. 92–93° (lit. 92–93°,[3] 93° [18]). After Jones' oxidation of basketane-9,10-diol in acetone and treatment with diazomethane only 12% of **26** could be isolated.

Hydrogenation of hydrocarbons **10**, **11** *and* **17**. Solutions of 20–60 mg of compounds in 10 ml n-pentane or MeOH and 20–60 mg of Pd–C were stirred magnetically under H_2 in a water bath at 20°. The uptake of H_2 was followed using a thermostatized burette. Samples were taken from time to time and analyzed by VPC on a capillary column 1 G 20 at 40°. The products were identified by comparison with authentic samples. The retention times are given in Table 2.

Table 2. Relative retention times in VPC analysis (*ca* 5–10 min)

Hydrocarbons on column:		Esters on column:	
1G20	40° injection 80°	DEGS	150° injection 180°
10	1.000	**24**	1.000
11	0.763	**25**	0.589
12	0.649	**27**	0.378
13	0.596	**29**	0.324
17	0.716	**26**	0.892
18	0.449	**28**	0.626
19	0.572	**30**	0.641
20	0.576		

Hydrogenation of **24** and **26**: 32.3 mg (0.15 mmol) of **24** were hydrogenated with 78 mg Pd–C in 10 ml n-pentane. After 95 h the product (28.5 mg) was 92% pure by VPC. Preparative VPC provided 11.4 mg (35%) of colourless crystals of **29**, m.p. 99–101° (lit.[15] 100–101°) and full agreement in all the spectra.

Compound **26** (172.5 mg, 0.78 mmol) with 100 mg Pd–C in 40 ml n-pentane were hydrogenated for 3 h and the product was separated by VPC (QF 1, 150°): yield 90.0 mg (52%) **28** with m.p. 63–63.5° (lit.[3] 61°) and full agreement in all the spectra and micro analysis.

Compound **26** (62.0 mg, 0.23 mmol) with 48 mg Pd–C in 20 ml MeOH was hydrogenated until uptake of H_2 stopped in 32 h. Preparative VPC (QF 1, 150°) of the product yielded 51 mg (81%) of a colourless oil in full accordance with an authentic sample of **30**,[16] spectra and micro analysis.

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