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Conformational Analysis. XCIX. The 1-Decalone Ring System[1,2]

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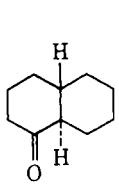
The equilibrium point for the isomerization of the 5α- and 5β-cholestan-4-ones has been redetermined to be 87 ± 1% 5α in ethanol at 25°, and earlier conflicting reports have been resolved. For the model 10-methyl-1-decalone system, the trans isomer is reported to be slightly favored at equilibrium, while, for the 9-methyl-1-decalone system, the cis isomer is favored. All of these results are well reproduced by a molecular mechanics calculation, and are discussed.

Twenty years ago Turner[3] was able to account quite well for the observed energy difference between *cis*- and *trans*-decalin, and to predict an energy difference between *cis*- and *trans*-9-methyldecalin (later verified experimentally[4,5]) in terms of the number of "gauche-butane"-like interactions in each isomer. The conformational analysis of decalone systems has presented a greater challenge, as numerous interactions between the carbonyl moiety and the rest of molecule have to be allowed for, including changes in the ring geometry due to the introduction of a carbonyl group. Early vector analysis calculations by Corey and Sneen[6] showed that these changes were likely to be important.

Klyne[7] sought to provide a systematic analysis of the interactions involved in decalone systems in terms of "alkyl ketone effects." His predictions concerning the conformational energies of 2-decalone systems have been borne out by experiments and recent force-field calculations.[8] In 1-decalone systems (1–9) he was able to account for the observed[9] stability of *trans*-1-decalone (1) as compared to *cis*-1-decalone (2, 3), and for the excess[10] of *cis*- (5, 6) over *trans*-9-methyl-1-decalone (4) at equilibrium. However, he calculated the *cis*-(a)-10-methyl-1-decalone conformer (9) to be of lower energy than *trans*-10-methyl-1-decalone (7), while the trans isomer is found experimentally to be the more stable. Since that time several equilibration studies have been carried out on 1-decalone systems[11-16] and steroidal analogs.[17-26] Conformational preferences have been deduced from ORD[27] and nmr[28] data, and these results have been discussed in terms of alkyl ketone effects.[29] Difficulties have persisted, particularly in reconciling the results reported for 1-decalone with those for steroidal analogs.



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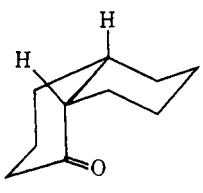

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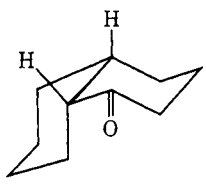

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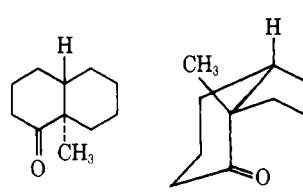
The advent of high-speed computers has permitted the application of molecular mechanics (or force-field) calculation methods to conformational problems. This approach explicitly allows for the relief of steric strain by distortion, and permits quantitative analysis of complex systems. In earlier papers in this series the method has been developed and applied to hydrocarbons,[30] ketones,[31,32] and other types of structures. The force field used for the present work differs only trivially from that described earlier.[32] An initial study of the 10-methyl-1-decalone system (7, 8, 9) by this method[31] showed that the observed $\Delta G°$ trans $\rightleftharpoons$ cis of ~0.2 kcal[14-16] could be accounted for.



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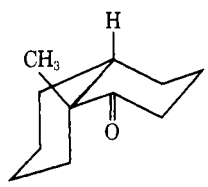

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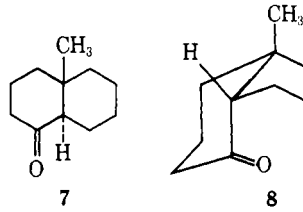

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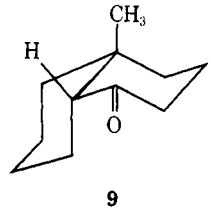
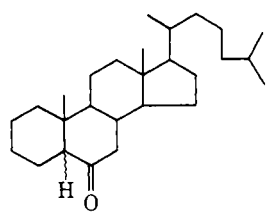
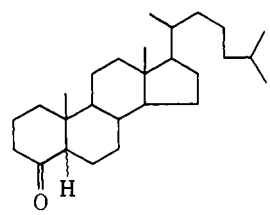


9

In an earlier paper in this series[17] on the cis $\rightleftharpoons$ trans equilibria of cholestan-6-ones (10, 11) and cholestan-4-ones (12, 13), experimental free-energy differences of 1.2 and 2.1 kcal, respectively, were reported. These values stand in marked contrast to the small $\Delta G°$ found in the 10-methyl-1-decalone system (above), and the reported preponderance of the cis epimer of 9-methyl-1-decalone at equilibrium.[10] The cholestan-4-one equilibrium (12, 13) can be considered to provide an experimental definition of



10, 5α
11, 5β



12, 5α
13, 5β

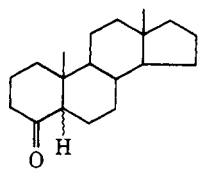
Table I
Heats and Free Energies of Isomerization (kcal/mol) for 1-Decalones[a]

Registry no.	Compd, conformer	$\Delta H°$ (trans ⇌ cis) Calcd	$\Delta H°$ (trans ⇌ cis) Exptl	$\Delta G°$ (trans ⇌ cis) Calcd	$\Delta G°$ (trans ⇌ cis) Exptl	Ref
493-02-7	*trans*-Decalin	0.0				
493-01-6	*cis*-Decalin	2.77	2.72 ± 0.20[c]			
21370-71-8	*trans*-1-Decalone (**1**)	0.0		0.0	0.0	38
32166-40-8	*cis*-1-Decalone (**2**)	1.97		1.85 (298)[h]	1.30[g]	12
	cis-1-Decalone (**3**)	2.87		1.77 (383)	1.15 (383)	13
				1.64 (493)	2.89 (493)	9
				1.61 (523)	2.30	
					3.10 (523)	11
2547-27-5	*trans*-9-Methyldecalin	0.0		0.0	0.0	
2547-26-4	*cis*-9-Methyldecalin	0.51	0.55 ± 0.28			5
			1.39 ± 0.64[f]			4
937-99-5	*trans*-9-Methyl-1-decalone (**4**)	0.0		0.0	0.0	
937-98-4	*cis*-9-Methyl-1-decalone (**5**)	0.13		−0.11 (298)		
	cis-9-Methyl-1-decalone (**6**)	0.53		−0.41 (523)	−0.37 (623)	10
937-77-9	*trans*-10-Methyl-1-decalone (**7**)	0.0		0.0	0.0	
770-62-7	*cis*-10-Methyl-1-decalone (**8**)	0.78[b]		0.42 (298)	0.21 (298)	15
	cis-10-Methyl-1-decalone (**9**)	0.89			0.21	
					0.10 (298)	14
				0.35 (350)	0.50 (350)	16
438-22-2	5α-Androstane	0.0				
438-23-3	5β-Androstane	0.84	0.89 ± 0.45			40
566-51-8	5α-Cholestan-4-one (**12**)	0.0		0.0	0.0	
6105-15-3	5β-Cholestan-4-one (**13**)	0.90[d]			1.10	
					1.20 (298)	
570-46-7	5α-Cholestan-6-one (**10**)	0.0		0.0	0.0	17, 24
13713-79-6	5β-Cholestan-6-one (**11**)	1.05[d]			1.16	
					1.25 (298)[g]	25
					1.12 (353)	24
					0.98	
					0.99 (373)	24
					1.05	
					1.08 (503)	24

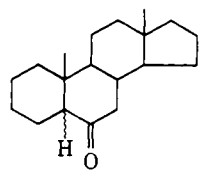
[a] In converting $\Delta H°$ figures to $\Delta G°$ terms symmetry numbers and optical activity effects are the same for all the bycyclic 1-decalone systesms (**1**–**9**). If a calculated $\Delta G°$ is not given, it is identical with the calculated $\Delta H°$ value. The calculated values for $\Delta H°$ are for individual conformations, while the $\Delta G°$ values are for the actual compounds, usually conformational mixtures. [b] *Cf.* 0.37 kcal (**8**), 0.70 kcal (**9**): ref 31. [c] A gas-phase $\Delta H°_{isom}$ of 3.17 kcal has been reported: ref 39. [d] Calculated values are for the androstanones (**14**–**17**). [e] Temperature not stated. [f] Heat of combustion data. [g] A $\Delta G°$ value of 1.06–1.13 is quoted for androstan-6-one in ref 25. [h] Temperature in °K.

an "*n*-butanal effect"[33] when compared to the hydrocarbon. In this case the 3-alkyl ketone and 2-alkyl ketone effects[7] are the same for the cis and trans isomers. The high value of $\Delta G°$ (trans ⇌ cis) found for cholestan-4-one was thus rationalized in terms of an *n*-butanal interaction of 0.88 kcal between the 4-ketone oxygen atom and the 7α hydrogen.[17] This figure was revised upward to 0.8–1.4 kcal/mol by Robinson.[33] Initial force-field calculations[31] on the *cis*-(e)-10-methyl-1-decalone (**8**) ("steroid" in the paper) structure failed to bear out this suggestion. The discrepancy between the equilibria of the steroid systems (**10**–**13**) and the 10-methyl-1-decalones (**7**–**9**), if 5β-cholestan-6-one (**11**) were taken to be a model for the low-energy cis conformer, has also remained to be accounted for.

Inspection of the literature since the reported equilibration of the cholestan-4-ones (**12**, **13**) to a mixture containing over 99% of the trans isomer reveals two reports at variance with this. Gutzwiller and Djerassi[18] report an equilibrium mixture containing ~90% of the trans isomer for the androstan-4-ones (**14**, **15**). Although large effects on the cis–trans equilibrium due to changes in the 17 substituent have been reported for ring A hydroxy-6-keto steroids,[26] in the absence of oxygen functionality in the side chain in either case it seemed unlikely[25] that this could account for the discrepancy. More recently, Robinson and Milewich[19] reported that an equilibration of cholestan-4-ones in refluxing methanol gave a mixture of 83% 5α- (**12**) and 17% 5β-cholestan-4-one (**13**) by tlc analysis, but details were sketchy.



14, 5α
15, 5β



16, 5α
17, 5β

A possible explanation for the contradictory reports in the steroid work was that the substance previously considered[17] to be 5α-cholestan-4-one was in fact a near-equilibrium mixture of the 5α and 5β isomers. It was decided, therefore, to prepare a sample of the compound by methods that would assure stereochemical purity, and remeasure the equilibrium.

In the previous equilibration study,[17] the sample of 5α-cholestan-4-one used was prepared from cholest-4-ene by a sequence of hydroboration, oxidation of the crude product with acetic acid–chromium trioxide, and chromatography on alumina. As 5β-cholestan-4-one was reported to epimerize on basic alumina, the possibility existed that cocrystallization of the 5α and 5β epimers had occurred, even though the sample was nicely crystalline, and the melting point behavior was judged to be satisfactory at the time. Pure samples of the cholestan-4-ones were therefore prepared, and the equilibrium was restudied.

Discussion

Cholest-4-ene was prepared from cholesterol by standard methods.[34,35] Hydroboration afforded a mixture of the epimeric 4 alcohols (72%). The mixture was partially

Table II
Optical Rotation Data for Pure Compounds[a,b]

Sample	Wavelength	[α]	n	m	s.d. (est)
5α-Cholestan-4-one (A)	307.5	−809.0	5	21	3.7
	267.0	1664.2	5	21	4.3
	Amplitude	2473.2			4.0
5α-Cholestan-4-one (B)	307.5	−813.8	1	8	0.4
	267.0	1668.7	1	8	1.4
	Amplitude	2482.5			1.0
Mean values	307.5	−811.4			2.6
	267.0	1666.5			3.2
	Amplitude	2478.4			2.9
5β-Cholestan-4-one	307.5	+352.6	3	11	6.6
	267.0	+256.5	3	11	8.5
	Amplitude	−96.1			

[a] n = number of separately weighed samples; m = number of ORD measurements; s.d. (est) = upper estimates of the variance in the mean rotations arising from the variance of the individual measurements. [b] See ref 42.

separated by column chromatography on alumina and fractional crystallization to give the known 5α-cholestan-4α-ol (27%) and a mixture of 5α-cholestan-4α-ol and 5β-cholestan-4β-ol (73%) as previously reported by Jones,[20] *et al.* Oxidation of 5α-cholestan-4α-ol under Jones conditions afforded 5α-cholestan-4-one. 5β-Cholestan-4-one was prepared both by fractional crystallization of the product of Jones oxidation of the mixed alcohols[20] and by BF_3-catalyzed rearrangement of 5α-cholestane 4α,5-epoxide.[36] The possibility that the 5α-cholestan-4-one might undergo epimerization under Jones oxidation conditions was ruled out by the observation that Jones oxidation of the mixed 5β-cholestan-4-ols from lithium aluminum hydride reduction of 5β-cholestan-4-one led to regeneration of the 5β-4 ketone. The two independent preparations of 5β-cholestan-4-one provide some assurance of the purity of the compound. The 5α- and 5β-4 ketones could be readily separated on tlc, and the samples used in the equilibration study were free from impurities by this criterion. The physical properties of the ketones are in accordance with previous reports. In particular the ORD curves reported here (Experimental Section) agree quite well with the data reported by Djerassi[37] for these compounds, deviations being generally in the sense of a greater magnitude of rotation.

An attempt to study the equilibrium by vpc was foiled by the facility of thermal isomerization[24] at the temperatures required for vpc (about 220°). However, the vpc study failed to reveal any components other than the epimeric cholestan-4-ones. Equilibrium was approached from both sides using acid and base catalysis at 25°, and the equilibrium mixtures were analyzed by ORD.[24] The mean rotations at 307.5 and 267 nm and the amplitude of the Cotton effect in each case are listed in Table II and III for the pure compounds and the equilibrium mixtures.

The equilibrium mixture of cholestan-4-ones (**12**, **13**) was estimated to consist of 87.4% (84.9–91.1%) 5α- (**12**) and 12.6% (8.9–15.1%) 5β-cholestan-4-one (**13**) (in ethanol at 25°). This agrees well with the reports of Djerassi[18] and Robinson[19] and also with the previously reported[17,24,25] result for the 6 ketone. It seems clear now that the sample of 5α-cholestan-4-one used in the earlier ORD measurements[17] was in fact an equilibrium mixture.

With this experimental discrepancy resolved we can now turn to the force-field calculations. Minimum energy all-chair conformations and their corresponding energies have been calculated for the 1-decalone structures (**1–9**) and the androstan-4-one (**14**, **15**) and androstan-6-one (**16**, **17**) structures as models of the cholestanone systems (**10–13**). This process has also been carried out for the parent hydrocarbons for comparison purposes. The calculated energy differences are found to be in reasonable agreement with the available experimental data in all cases. (See Table I).

The question of the high percentage of the cis isomer in the equilibrium mixtures of the bicyclic 1-decalone compounds (**1–9**) compared with the steroidal analogs (**10–17**) is now largely resolved by noting that there are two different low-energy cis conformers, cis equatorial (**2**) and cis axial (**3**), accessible in each of the bicyclic *cis*-1-decalone

Table III
Optical Rotation Data For Equilibrium Mixtures

Sample, reagent	Wavelength	[α]	n	m	s.d. (est)	Est % 5β	C[a]
5α-Cholestan-4-one (A)							
Base	307.5	−658.8	2	16	5.1	13.1 ± 0.5[b]	1.04
	267.0	1453.8			6.7	15.1 ± 0.5	
	Amplitude	2112.5			8.4	14.2 ± 0.3	
Acid	307.5	−654.8	3	24	3.6	13.5 ± 0.4	1.02
	267.0	1464.3			5.7	14.3 ± 0.4	
	Amplitude	2119.1			5.9	14.0 ± 0.2	
5α-Cholestan-4-one (B)							
Base	307.5	−672.9	2	16	5.1	11.9 ± 0.5	1.01
	267.0	1489.0	2	12	7.0	12.6 ± 0.5	
	Amplitude	2162.3	2	12	8.6	12.3 ± 0.3	
Acid	307.5	−682.2	1	4	7.6	11.1 ± 0.7	0.96
	267.0	1540.5	1	4	9.4	8.9 ± 0.7	
	Amplitude	2222.7	1	4	12.1	9.9 ± 0.5	
5β-Cholestan-4-one							
Base	307.5	−662.4	3	16	5.7	12.8 ± 0.5	1.03
	267.0	1467.0			13.7	14.1 ± 1.0	
	Amplitude	2129.4			14.6	13.6 ± 0.6	
Acid	307.5	−671.4	3	20	4.5	12.0 ± 0.4	0.98
	267.0	1507.9			14.1	11.2 ± 1.0	
	Amplitude	2179.3			14.3	11.6 ± 0.6	
Mean values	307.5					12.4 ± 0.5	
	267.0					12.7 ± 0.9	
	Amplitude					12.6 ± 0.7	

[a] C = volumetric correction factor necessary if observed rotations were due to a mixture of pure 5α- and 5β-cholestan-4-one. [b] Estimated standard deviation in the estimated percentage of 5β-cholestan-4-one arising from variance in rotations.

systems (2, 3; 5, 6; 8, 9) and only one in each of the steroid cases (11, 13, 15, 17). The recent report by House[41] that the equilibrium mixture of *cis*- and *trans*-7α-*tert*-butyl-1-decalone contains only about 5% of the cis compound is in keeping with this interpretation, as only one low-energy cis conformer is accessible in this system. This statistical effect is sufficient to result in an excess of *cis*-9-methyl-1-decalone (5, 6) in the calculated equilibrium mixture at room temperature, despite the slightly lower steric energy for the trans isomer 4 (in contrast to Klyne's early prediction[7]).

Very little experimental information is available on the conformational preferences of the *cis*-1-decalone systems. Djerassi has concluded from ORD data[27] that the cis axial conformer (9) is favored in *cis*-10-methyl-1-decalone, and the cis equatorial conformer is favored in both *cis*-1-decalone (2) and *cis*-9-methyl-1-decalone (5). Guy and Wintermitz[28] have adduced nmr data to support the latter conclusion. The calculations predict the cis equatorial conformer to be favored in each case (2, 5, 8), but for the angular methyl compounds the energy difference is slight, and substantial amounts of each conformer are predicted at room temperature.

Zalkow,[43] *et al.*, have shown that ketal formation in steroid 3 ketones can be quantitative in anhydrous acidic alcohol solutions. Ketal formation was found to be less extensive in ethanol than in methanol, to be significantly decreased by an equatorial alkyl substituent adjacent to the ketone, and to be very sensitive to added water. In 95% ethanol–water the extent of ketal formation under acid-catalyzed equilibration conditions should be less than 0.5%. Precautions were taken against condensation and oxidation side reactions under basic equilibration conditions.

The rotations listed in Tables II and III are the mean values for several sets of measurements as indicated, and the standard deviations quoted are (upper) estimates of the standard deviation in the mean arising from the variance in and between the individual measurements. Some of the values differ by large amounts compared to the estimated standard deviations, so that systematic errors cannot be completely ruled out. However, varying the time for equilibration showed no effects attributable to side reactions, and the two samples of 5α-cholestan-4-one which gave slightly different equilibration results gave ORD curves which were identical within experimental limits.

Estimated equilibrium compositions are listed in Table III in terms of the percentage of 5β-cholestan-4-one, for the different samples and reaction conditions. Analysis of the errors showed that to a first approximation proportional errors were large compared to constant errors in the rotations. Thus the determination at 307.5 nm is inherently more accurate, as the rotation change is the greatest at this wavelength.

Conclusions

The present work removes the previous inconsistencies concerning the stabilities of 1-decalone ring systems, and is in agreement with our earlier conclusion, that force-field calculations can give results with accuracy competitive with experiment for molecules and properties such as discussed here, and any serious difference between calculation and experiment does not necessarily reflect on the accuracy of the calculation, but may well be the fault of the experiment.

Experimental Section

Melting points were determined with a Fisher-Johnson hot-stage apparatus. Optical rotatory dispersions were measured with a Cary 60 recording spectropolarimeter.

Cholestan-4-ols.[20,44] To a stirred solution of 5 g (13.5 mmol) of cholest-4-one[35] (prepared from cholest-4-en-3-one[34]) in 50 ml of tetrahydrofuran at 0° was added a solution of diborane (about 25 mmol) in 25 ml of tetrahydrofuran. The reaction mixture was stirred at room temperature for 1 hr. Excess reagent was quenched by the addition of 2 ml of water; then 3 ml of 3 *N* aqueous NaOH was added, followed by 20 ml (233 mmol) of 30% hydrogen peroxide. The mixture was stirred at room temperature for 2 hr and extracted with ether. The ether extract was washed with water, acidified aqueous potassium iodide solution, aqueous sodium thiosulfate solution, dilute aqueous sodium bicarbonate solution, water, and saturated aqueous NaCl, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. Column chromatography of the residue on neutral alumina (activity IV) followed by fractional crystallization from methanol–ether yielded 1.0 g (21.3%) of 5α-cholestan-4α-ol, mp 188–189°, $[\alpha]^{26}D$ +4.4 + 0.2° (*c* 0.959, $CHCl_3$) (lit.[44] mp 187–188°, $[\alpha]D$ +3°). The remaining material (2.7 g) was a mixture of 5α-cholestan-4α-ol and another component, presumably[20] 5β-cholestan-4β-ol (51.4%) by tlc and vpc.

5α-Cholestan-4-one. To a stirred solution of 1.02 g (2.6 mmol) of 5α-cholestan-4α-ol in 50 ml of acetone (Baker Analyzed) at room temperature, 8 *M* chromic acid was added dropwise until a permanent red color appeared. The mixture was stirred for 10 min, and the reaction was quenched with saturated aqueous sodium metabisulfate solution. The mixture was added to 200 ml of water and extracted twice with ether. The ether extracts were washed with water, dilute aqueous sodium bicarbonate solution, again with water, and saturated aqueous NaCl, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the residue was combined and crystallized from methanol–ether to yield 0.60 g (59%) of 5α-cholestan-4-one: mp 98–100° (lit.[45] mp 99–99.5°); ORD (95% C_2H_5OH) $[\alpha]_{267}$ +1664° (max), $[\alpha]_{307.5}$ 809° (min) [lit.[46] ORD $[\alpha]_{267.5}$ +1650° (max), $[\alpha]_{307.5}$ −780° (min)].

5β-Cholestan-4-one. To a stirred solution of 1.2 g (3.1 mmol) of mixed cholestan-4-ols (predominantly 5β-cholestan-4β-ol by tlc and vpc) in 50 ml of acetone (Baker Analyzed) at room temperature, 8 *M* chromic acid was added dropwise until a permanent red color appeared. The mixture was stirred for 10 min, and the reaction was quenched with saturated aqueous sodium metabisulfite solution. The mixture was added to 200 ml of water and extracted twice with ether. The ether extracts were washed with water, dilute aqueous sodium bicarbonate solution, with water again, and with saturated NaCl solution, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the combined residues were crystallized from methanol–ether, yielding 0.65 g (54%) of 5β-cholestan-4-one: mp 110–111° (lit.[37] mp 111–112°); ORD (95% C_2H_5OH) $[\alpha]_{309}$ +350.9° (max), $[\alpha]_{304}$ +344.2° (min), $[\alpha]_{299}$ +360.3°, $[\alpha]_{275}$ +233.4° [lit.[37] ORD $[\alpha]_{300}$ +318° (max), $[\alpha]_{277.5}$ +240° (min)].

5β-Cholestan-4-one.[36] To a solution of 5α-cholestane 4α,5-epoxide (210 mg, 0.543 mmol) in dry benzene (30 ml) at room temperature was added BF_3–Et_2O (0.375 ml, 325 mg, 2.29 mmol, distilled off CaH_2). The reaction was quenched after 50 sec by the addition of aqueous Na_2CO_3. The crude product, isolated with ether, was crystallized repeatedly from methanol–ether to give 5β-cholestan-4-one (66 mg, 0.171 mmol, 31%) as needles, mp and mmp 108–109°.

5α-Cholestane 4α,5-Epoxide. To a solution of cholest-4-ene (0.25 g, 0.675 mmol) in dry ether (10 ml) at 0° was added a solution of monoperphthalic acid (20 mmol) in ether (10 ml). The reaction mixture was allowed to stand at 0° for 4 days and quenched with aqueous $NaHCO_3$. The ether layer was separated, washed with dilute aqueous $NaHCO_3$ and water, and dried over saturated aqueous NaCl and anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure and repeated crystallization from acetone gave 5α-cholestane 4α,5-epoxide (110 mg, 0.285 mmol, 42%), mp 98–99° (lit.[21] mp 100–101°).

A Preliminary Test of the Modified Jones Oxidation Conditions. Preparation of 5β-Cholestan-4-ol and Regeneration of 5β-Cholestan-4-one. One gram of 5β-cholestan-4-one (mp 108°) in ether was added dropwise to a slurry of ether and 1 g of $LiAlH_4$. The reaction mixture was stirred at room temperature overnight. The excess $LiAlH_4$ was destroyed by water under a nitrogen atmosphere. Saturated ammonium chloride solution was then added, the reaction mixture was filtered, and the filtrate was extracted with ether and dried over anhydrous sodium sulfate. After removal of the ether, the white solid residue (0.95 g) showed two spots on thin layer chromatography (R_f 19, 26 in ethyl acetate), which were interpreted as

the axial and equatorial alcohols resulting from the $LiAlH_4$ reduction. The infrared spectrum showed hydroxyl stretching but no carbonyl stretching. Since both the coprostan-4α-ol and the coprostan-4β-ol would yield the same ketone, coprostan-4-one, upon oxidation, the alcohol mixture was not separated or purified any further.

The crude alcohol mixture (1.4 g, 3.2 mmol) was dissolved in 300 ml of acetone and oxidized at 19–21° by adding 1.6 ml of 8 *N* chromic acid reagent dropwise during 45 min. The solution was allowed to stand for 3 hr, and then was poured into water. The precipitate was collected and taken up in $CHCl_3$. The chloroform layer was washed and dried, and the solvent was evaporated *in vacuo*. The product was recrystallized from acetone, yield of 1.2 g, mp and mmp with authentic sample (mp 108°) 106°.

Equilibration of the Ketones. Standard solutions of the ketones were prepared by use of a Mettler H20 T balance and calibrated graduated flasks. Solutions were kept in a thermostat at 25° throughout. The ORD curves for the pure ketones were recorded for solutions in 95% ethanol (previously distilled off NaOEt to remove traces of aldehydes), in a jacketed 1-cm quartz cell at 26.3–26.4°. Solutions of the ketones were made up in the same way, except that 0.1 *M* KOH in ethanol or about 0.1 *M* HCl in ethanol were used instead of ethanol. Equilibrations were allowed to proceed at 25° under nitrogen. Concentrations were chosen to give the greatest possible amplitude on the recording chart on the 1° scale (about 60 mg in 10 ml for 5α-cholestan-4-one; about 20–30 mg in 10 ml for the less soluble 5β-cholestan-4-one). ORD curves were measured for the equilibrating solution after 3 hr for the base-catalyzed equilibrations, and after 7 days for the acid-catalyzed equilibrations. The amplitude of the Cotton effect and the magnitude of the rotation at 267 and 307.5 nm was recorded in each case, and the percentage of 5β-cholestan-4-one in the equilibrium mixture was calculated in the usual manner.[24]

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Chemistry of Some Tricyclic Cyclopropyl Halides

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The silver ion assisted methanolysis of **2**, **3**, and **4** has been studied. Both rates and products are reported. Comments are made as to the effect of neighboring sites of unsaturation on relative reactivities. The effect of complexed silver ion on reactivity is also discussed.

The chemistry of cyclopropyl systems of the general type **1** has been the subject of several recent studies.[2-7] Herein we report on the chemistry of systems of this type, namely, the silver ion assisted solvolysis of **2**, **3**, and **4**. Our immediate goal was to ascertain the reaction pathways available to systems in which the normal disrotatory