

483. *Steroids and Walden Inversion. Part XXXII.**
The 3 : 5-cycloSteroid Rearrangement.

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Determination of the heats of combustion at 25° of cholesteryl methyl ether and 3 : 5-cyclocholestan-6 β -yl methyl ether shows that the former is energetically more stable by 5.7 kcal./mole, and confirms the assumption made by Shoppee and Summers¹ to explain the experimental facts relating to the 3 : 5-cyclosteroid rearrangement.

Calculation of resonance energies and compression energies for the cholest-5-enyl cation with progressive deformation corresponding to various C₍₃₎-C₍₅₎ distances, and recalculation of the resonance energies given by Simonetta and Winstein,⁴ suggest that the 3 : 5-cyclosteroid rearrangement takes place through a non-classical mesomeric cation.

SOME years ago Shoppee and Summers¹ suggested that the 3 : 5-cyclosteroid rearrangement (I \rightleftharpoons II) was explicable on the assumption (a) that the Δ^5 -molecule is thermodynamically more stable than the isomeric 3 : 5-cyclo-molecule, and (b) that the transition state for the ionic recombination : Δ^5 -cation \longrightarrow Δ^5 -molecule, is of higher energy than that for the ionic recombination : 3 : 5-cyclo-cation \longrightarrow 3 : 5-cyclo-molecule. This suggestion was illustrated by a symbolic energy diagram (Fig. 1); in brief, kinetic control of the reactions should lead to formation of 3 : 5-cyclosteroid as sole product, whilst thermodynamic control of the equilibria should eventually lead to formation of Δ^5 -steroid as sole product.

Through the kindness of Dr. D. D. Wagman of the Thermochemistry Section of the National Bureau of Standards, Washington, U.S.A., experimental evidence can now be adduced in support of assumption (a) from measurements of the heats of combustion at 25° of cholesteryl methyl ether (I; X = OMe) and 3 : 5-cyclocholestan-6 β -yl methyl ether (II; Y = OMe).

Since ΔH°_c represents the change in heat content when 1 mole of the substance reacts

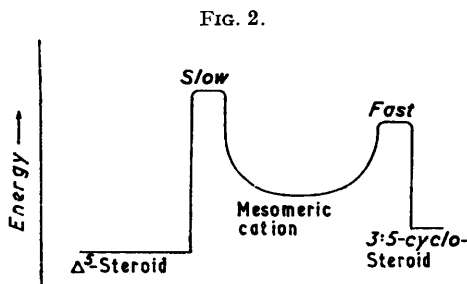
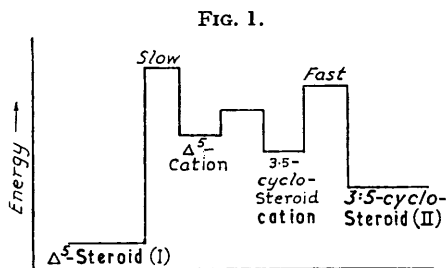
* Part XXXI, *J.*, 1956, 1893.

¹ Shoppee and Summers, *J.*, 1952, 3361.

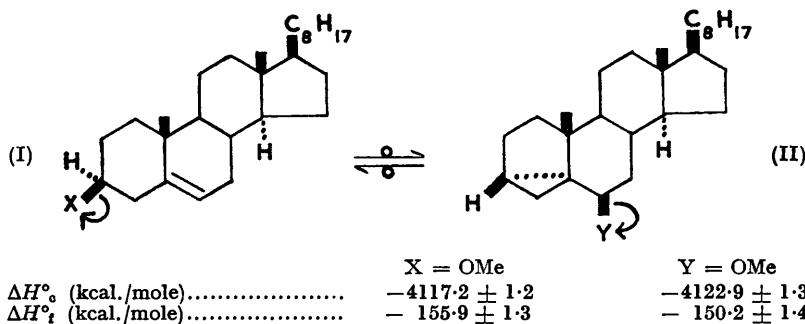
with oxygen (in the ideal-gas state) to form carbon dioxide (in the ideal-gas state) and liquid water, all at one atmosphere pressure, and ΔH°_f represents the heat of formation of 1 mole of substance from graphite, hydrogen, and oxygen, all at one atmosphere pressure, it will be seen that cholesteryl methyl ether (I; X = OMe) is energetically more stable at 25° than 3:5-cyclocholestan-6 β -yl methyl ether (II; Y = OMe) by 5.7 kcal./mole. This is very close to the value of 7 kcal./mole estimated by Roberts, Trumbull, Bennett, and Armstrong² from the difference between the heats of combustion of propene and cyclopropane.

In the original paper,¹ a second symbolic energy diagram (Fig. 2) corresponding to a non-classical mesomeric cation, as opposed to two classical isomeric cations, was given; on the available evidence, it appeared impossible to distinguish between the two alternatives. In 1952, we attempted to calculate, by a semi-empirical molecular-orbital method, the compression energies required to deform the cation corresponding to the molecular structure (I) so that the 3-hydrogen atom occupies a mean position and to compute the resonance energy of the system.

In cholest-5-enes ring A is a slightly strained chair-form with C₍₃₎ lying a little behind the plane of C₍₄₎, C₍₅₎, C₍₆₎, and C₍₁₀₎; ³ this geometry should persist in the cation, although introduction of *sp*² hybridisation at C₍₃₎ will lead to adoption by the 3-hydrogen atom of a



position of trigonal symmetry. 3:5-Interaction with decrease of the C₍₃₎—C₍₅₎ distance in the cation could occur in two ways: (a) by approach of C₍₃₎ to the plane of C₍₄₎, C₍₅₎, C₍₆₎, and C₍₁₀₎ (which on a model is surprisingly easy) and subsequent deformation of the



3-4-5 bond angle, (b) by recession of C₍₃₎ from the plane of C₍₄₎, C₍₅₎, C₍₆₎, and C₍₁₀₎ along a curve defined by the length (assumed constant) of bond 3-4 with deformation of the 3-4-5 bond angle. In (a) the axes of the vacant *p*-orbital of C₍₃₎ and the *p*-orbital of C₍₅₎ become parallel, and our calculations (see Appendix) confirm that 2*pπ* overlap is very small at all probable C₍₃₎—C₍₅₎ distances, whilst the corresponding compression energies are considerable (see Table 1). In (b) the axes of the vacant *p*-orbital of C₍₃₎ and the *p*-orbital of C₍₅₎ intersect at 60° and this angle tends to increase with decrease of the C₍₃₎—C₍₅₎

² Roberts, Trumbull, Bennett, and Armstrong, *J. Amer. Chem. Soc.*, 1950, **72**, 3116.

³ Cremllyn, Rees, and Shoppee, *J.*, 1954, 3790.

distance. Our calculations here were forestalled by Simonetta and Winstein,⁴ who showed that $2p\pi$ overlap becomes large enough to be of some chemical importance at the normal $C_{(3)}-C_{(5)}$ separation of 2.5 Å. The strain energy formula for various $C_{(3)}-C_{(5)}$ distances used by Simonetta and Winstein is similar in form to that used by us in (a), but in their calculations they adopted alternative values for the carbon-carbon single-bond energy of 59 and 66 kcal./mole. We have recalculated their strain energies using the more probable value⁵ of 84.4 kcal./mole (Table 2). A maximum stabilisation of 4–5 kcal./mole is attained

TABLE 1.

$C_{(3)}-C_{(5)}$ distance (Å)	2.5	2.4	2.3	2.2	2.1	2.0	1.9	1.8	1.7	1.6
Resonance energy (kcal./mole)	0	0	0	0	-0.12	-0.30	-0.78	-1.68	-3.44	-7.32
Compression energy (kcal./mole)	0	+0.5	+1.7	+3.7	+6.6	+10.5	+15.3	+21.3	+28.1	+35.9

TABLE 2.

$C_{(3)}-C_{(5)}$ distance (Å)	2.5	2.35	2.15	1.95	1.75	1.63	1.54
Resonance energy (kcal./mole), } Simonetta & Winstein	-1.8	-4.2	-8.3	-13.2	-17.4	-18.8	-19.7
Strain energy (kcal./mole)	0	+1.2	+3.9	+8.9	+14.7	+18.6	+21.2
Total energy (kcal./mole)	-1.8	-3.0	-4.4	-4.3	-2.7	+0.2	+1.5

at a $C_{(3)}-C_{(5)}$ distance of ~ 2.1 Å (cf. Simonetta and Winstein's figure of 1.75–1.95 Å). In agreement with experimental evidence on the facility of the 3 : 5-cyclosteroid rearrangement, there appears to be significant stabilisation of the positive charge at $C_{(3)}$ by delocalisation of the π -electrons of the 5 : 6-double bond for a compression of the $C_{(3)}-C_{(5)}$ distance of about 0.4 Å. The calculations thus support the conception of a non-classical mesomeric cation (Fig. 2), although the formation of a cyclopropane ring eventually requires a σ -bond rather than a π -bond between $C_{(3)}$ and $C_{(5)}$.⁶

APPENDIX

The resonance integral β_1 of the 3–5-bond for various $C_{(3)}-C_{(5)}$ distances was calculated from the equation of Lennard-Jones,⁷ $2\beta_{(r)} = \Delta + C_{s(r)} - C_{a(r)}$, on the assumption of its validity for bond lengths greater than 1.54 Å. The resonance integral β_2 of the 5 : 6-bond was given a value of 42.4 kcal. corresponding to a π -bond order of 0.98, which is the value it assumes by resonance of the 5 : 6 π -bond and a 3 : 5 π -bond of length 1.8 Å. The resonance integrals β_1 and β_2 were substituted in the secular equation :

$$(\alpha_r - \epsilon)c_x + \sum' y\beta_{xy}c_y = 0 \quad (x = 1, 2, 3)$$

to give the total π -electron energy ϵ . The resonance energy for each electron is the difference between ϵ and the initial π -electron energy β_2 , and since there are two $2p\pi$ -electrons the required resonance energy is $2(\epsilon - \beta_2)$.

$C_{(3)}-C_{(5)}$ distance (Å)	2.1	1.9	1.8	1.7	1.6	1.5
β_1	2.25	5.8	8.45	12.2	18.0	25.2
β_2	42.4	42.4	42.4	42.4	42.4	42.4
ϵ	42.46	42.79	43.24	44.12	46.06	49.32
Resonance energy (kcal./mole)	-0.12	-0.78	-1.68	-3.44	-7.32	-13.84

In our calculations of compression energies, we have assumed that the 2–3–4 bond angle remains constant and the $C_{(3)}-C_{(4)}$ and $C_{(4)}-C_{(5)}$ distances remain unchanged; the terms computed are those involving deformation of the bond angles 1–2–3, 3–4–5, and 4–5–10, and l , the stretching of the 2 : 3-bond. Deformation of the bond angle 1–2–3 leads to a decrease in the

⁴ Simonetta and Winstein, *J. Amer. Chem. Soc.*, 1954, **76**, 18.

⁵ Roberts and Skinner, *Trans. Faraday Soc.*, 1949, **45**, 339.

⁶ Coulson and Moffitt, *Phil. Mag.*, 1949, **40**, 1.

⁷ Lennard-Jones, *Proc. Roy. Soc.*, 1937, *A*, **158**, 297.

overlap of the appropriate sp^3 orbital of $C_{(2)}$ with the corresponding sp^2 orbital of $C_{(3)}$ and to reduction of the strength of the 2 : 3-bond; the component of the sp^3 orbital directed along the 2 : 3-bond is $\frac{1}{2} + \frac{3}{2} \cos 0^\circ = 2$, and in the new direction 2-3' is $\frac{1}{2} + \frac{3}{2} \cos \alpha$, where α is the angle by which 1-2-3 is distorted. Since the bond angle 2-3-4 is assumed to be constant, the component of the sp^2 orbital, initially directed along the 3 : 2-bond, remains unchanged along the 3' : 2-bond at $\sqrt{\frac{1}{3}} + \sqrt{2} \cos 0^\circ = 1.99^*$. Taking the strength of a C-C single bond to be B ($= 84.4$ kcal./mole.) and assuming that the strength of a bond is proportional to the overlap of the orbitals, we find that the strength of the 2 : 3-bond is $B(2 \times 1.99)/(2 \times 2) = \sim B$ because the "orbital strength" of each sp^3 orbital component of a carbon-carbon single bond is 2^* . Similarly, the strength of the 2 : 3'-bond is $B[1.99 \times (\frac{1}{2} + \frac{3}{2} \cos \alpha)]/(2 \times 2) = \sim B(\frac{1}{2} + \frac{3}{2} \cos \alpha)/2$, and the energy required to deform the bond angle 1-2-3 by an angle α is

$$B \left[\frac{1.99}{2} - \frac{1.99(\frac{1}{2} + \frac{3}{2} \cos \alpha)}{4} \right] = \sim 3B(1 + \cos \alpha)/4.$$

Deformation of the bond angles 3-4-5 and 4-5-10 results in decrease in the strength of 3 : 4- and 4 : 5-bonds. The components of the sp^3 orbitals of $C_{(4)}$ along the 4 : 3- and 4 : 5-bonds are both $\frac{1}{2} + \frac{3}{2} \cos 0^\circ = 2$, and in the new directions 4'-3' and 4'-5 are both $\frac{1}{2} + \frac{3}{2} \cos \beta$, where 2β is the angle by which the angle 3-4-5 is deformed. As the bond angle 2-3-4 is assumed to be constant, the sp^2 orbital of $C_{(3)}$, which initially had its maximum component along the 3 : 4-bond, now has its maximum component along the 3' : 4'-bond and equal to $\sqrt{\frac{1}{3}} + \sqrt{2} \cos 0^\circ = 1.99^*$. The component of the sp^2 orbital of $C_{(5)}$ along the 5 : 4-bond is $\sqrt{\frac{1}{3}} + \sqrt{2} \cos 0^\circ = 1.99^*$, *i.e.*, ~ 2 , and in the new direction 5-4' is $\sqrt{\frac{1}{3}} + \sqrt{2} \cos \beta$, since β is the angle by which the bond angle 10-5-4 is deformed. By a similar argument to that used for the bond angle 1-2-3, the energy required to deform the bond angles 3-4-5 and 4-5-10 is :

$$B \left[\frac{1.99}{2} - \frac{1.99(\frac{1}{2} + \frac{3}{2} \cos \beta)}{4} \right] = \sim 3B(1 + \cos \beta)/4,$$

and

$$B \left[\frac{1.99}{2} - \frac{(\sqrt{\frac{1}{3}} + \sqrt{2} \cos \beta)(\frac{1}{2} + \frac{3}{2} \cos \beta)}{4} \right] = \sim B(1 - (\sqrt{\frac{1}{3}} + \sqrt{2} \cos \beta)(\frac{1}{2} + \frac{3}{2} \cos \beta))/4.$$

* The values used for the variation of bond strength with hybridisation are those given by Pauling and Sherman⁸ which make $sp^3 > sp^2 > sp$, although there is now evidence⁹ that the correct order is $sp < sp^2 < sp^3$.

$C_{(3)}-C_{(5)}$ distance (Å) ...	2.5	2.4	2.3	2.2	2.1	2.0	1.9	1.8	1.7	1.6
α	0	4	8	11	15	18	21	25	28	30
β	0	3	6	9	11.5	14	16	19	21	23
l	0	~ 0	0.01	0.03	0.05	0.08	0.11	0.15	0.20	0.25
Compression energies										
1-2-3	—	0.2	0.6	1.2	2.1	3.2	4.4	5.8	7.2	8.8
3-4-5 and 4-5-10 ...	—	0.3	1.0	2.2	3.7	5.5	7.5	9.8	12.2	14.8
l	—	0.0	0.1	0.3	0.8	1.8	3.4	5.7	8.7	12.3
Total	0	0.5	1.7	3.7	6.6	10.5	15.3	21.3	28.1	35.9

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⁸ Pauling and Sherman, *J. Amer. Chem. Soc.*, 1937, **59**, 1450.

⁹ Maccoll, *Trans. Faraday Soc.*, 1950, **46**, 369.