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THE SYNTHESIS OF REGIOSOMERIC CYCLOBUTANONES BY CARBONYL TRANSPOSITION. CONFORMATION OF FUSED CYCLOBUTANONES.[1a]

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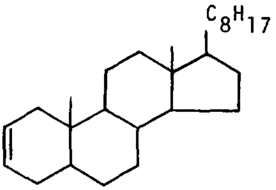
In a preliminary communication,[2] we reported that dichloroketene adds to 2-cholestene (1) in a highly regioselective[3] manner to give the dichlorocyclobutanone 2b. In our work concerning the possible application of circular dichroism (CD) to stereochemical assignments and conformational studies of fused steroidal cyclobutanones, we became interested in converting the readily available dichlorocyclobutanone 2b to the cyclobutanones 3.



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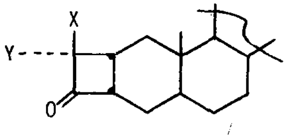
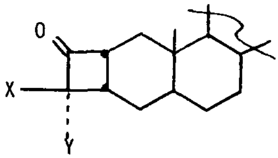


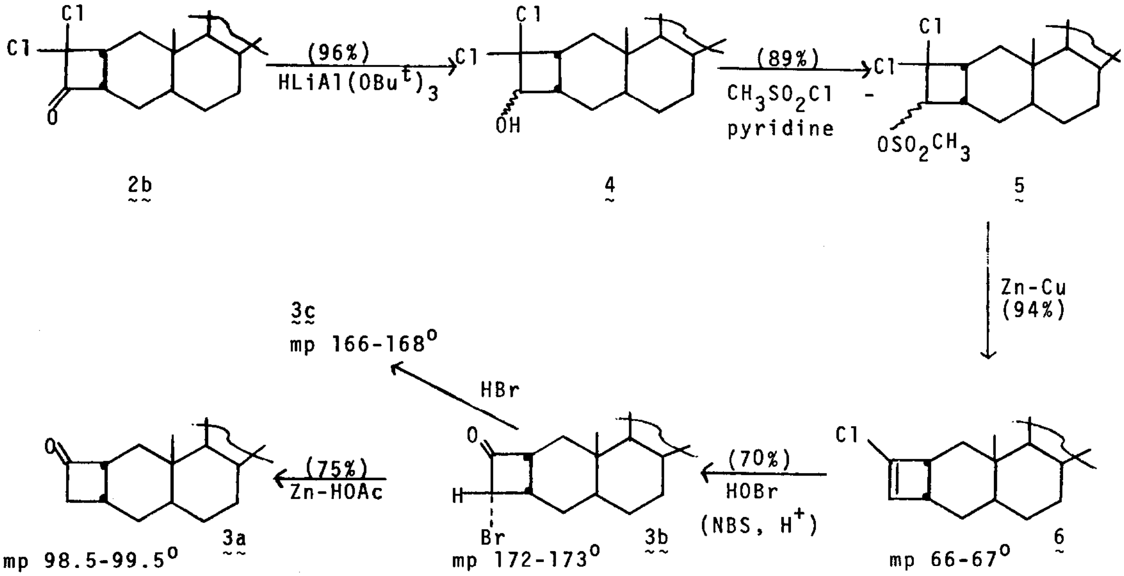
2a, X, Y=H
2b, X, Y=Cl



3a, X, Y=H
3b, X=H, Y=Br
3c, X=Br, Y=H

We would like to report an efficient method for transposing the carbonyl group in cyclobutanone 2b to its regioisomeric position in 3. Although several steps are required (2b→4→5→6→3b) the overall yield is good (57% overall). The crude alcohol 4 and the crude mesylate 5 can be used without purification to give the pure vinyl chloride 6 (82% overall).[4] The addition of hypobromous acid (NBS, H^+) to 6 proceeded smoothly to give 3b which contained only a trace (via tlc) of the isomer 3c. Recrystallization (ethyl acetate - ethanol) gave 3b pure in 70% yield.

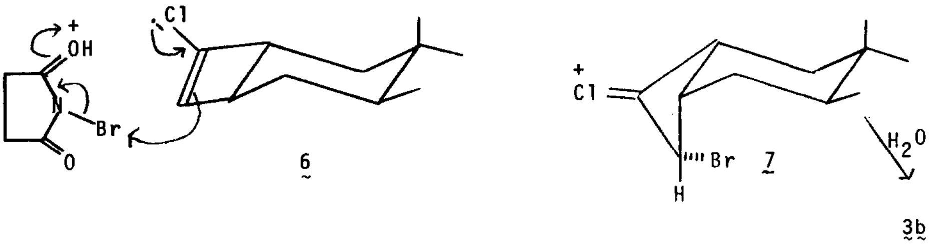
The formation of a bromohydrin from treatment of an alkene with N-bromosuccinimide and acid is believed to proceed by an electrophilic attack of the protonated bromoamide upon the olefin.[5] Such an attack generally occurs from the less



nmr, τ4.9 (d of d, 1, O=CCHBr)

nmr, τ4.2 (s, 1, vinyl H) and τ6.9 (m, 2, allylic H)

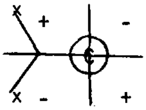
hindered side of the double bond[6] and models indicate that the β-side of the vinyl chloride **6** is less sterically hindered than the α-side.



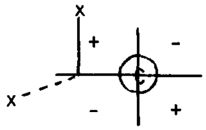
The surprising formation of **3b** as the kinetic product is best explained in terms of stereoelectronic control during bromination of **6** leading preferentially to the pseudoaxial bromide **7**. That **3b** is not the thermodynamic product was shown by its clean conversion to the equatorial bromo ketone **3c** on equilibration with HBr-acetic acid (**3b** and **3c** are clearly different compounds by tlc and mixed mp, 140-155°). The nmr (doublet of doublets at τ4.9, indicative of a proton geminal to Br and α to the carbonyl for **3b** and **3c**), ir (1787 and 1792 cm^{-1} respectively for **3b** and **3c**), and CD data (See table) were consistent with the assigned structure.

Dichloroketene adds to both activated and nonactivated olefins in fair to good yield, to give cyclobutanones which are useful synthetic intermediates.[8] Since all reported additions of dichloroketene to olefins show complete regiospecificity, the route we have outlined here makes the other keto isomer available. Furthermore, since attempts to brominate ketone 3a were unsuccessful,[9] the route discussed provides a useful path to the bromoketones, 3b and 3c as well. The formation of the vinyl chloride 6 in high yield (82% overall) also suggests the adaptibility of our scheme to a useful cyclobutene synthesis.

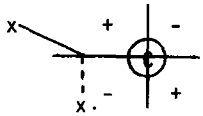
Although a preference of cyclobutanes toward the nonplanar conformation is quite well established there is still some uncertainty concerning the geometry of the cyclobutanone ring.[10] Our circular dichroism studies allow a clear differentiation between the planar 8 and the two puckered conformers 9 and 10 of the fused cyclobutanone ring in 2. In the planar conformation 8 the effect of the two halogens in opposite quadrants should cancel each other. This is not true for conformers 9 and 10. The molecular elipticity of 2b and its dechlorinated derivative 2a (see Table I) clearly indicates a preference for conformer 9.



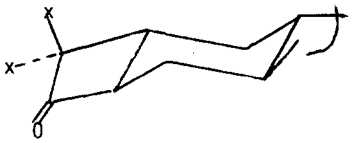
planar conformer 8



conformer 9



conformer 10



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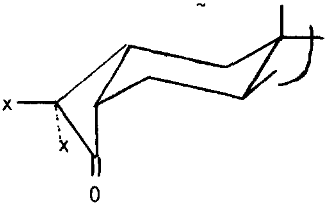

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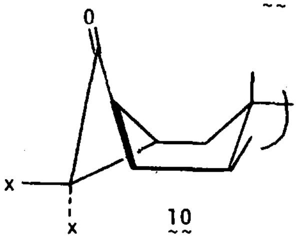

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Table 1

Circular Dichroism Data on Steroidal A- Fused Cyclobutanones

ketone	configuration of halogen	molecular elipticity [θ]
2a	-	+ 2,500
2b	a,e	+24,000
3a	-	-12,000
3b	a	+ 4,000
3c	e	- 6,100

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