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A NEW REARRANGEMENT IN THE REACTION OF α,α-DIHALOCYCLOBUTANONES WITH BASE[1]

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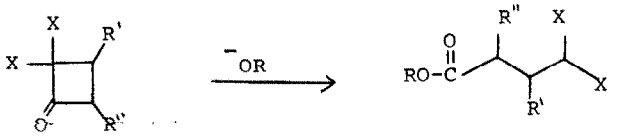
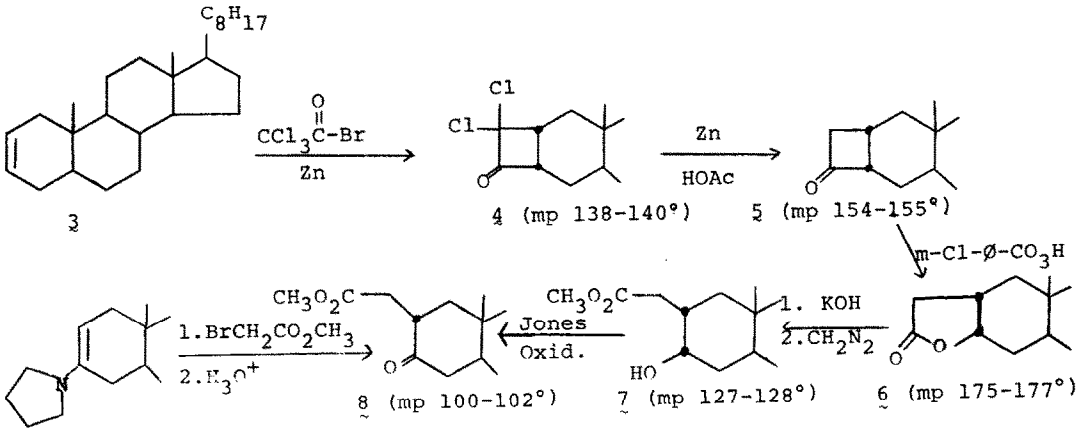
We would like to report a new rearrangement in the reaction of α,α-dichlorocyclobutanones with sodium methoxide leading to a bifunctional cyclopropane. The reported reaction[2] of α,α-dihalocyclobutanone 1 with base is ring-cleavage to the dihalocarboxylic compound 2.



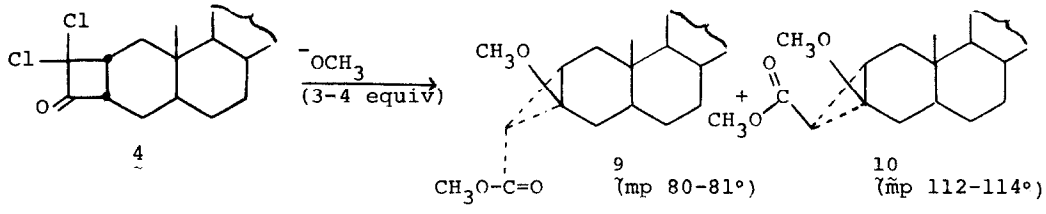
1 2

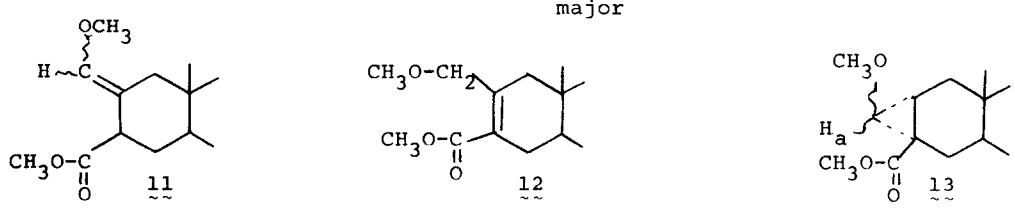
We found that the addition of dichloroketene to 2-cholestene (3) proceeds in a highly regioselective[3] manner to give the cyclobutanone 4 in 75% yield. The regiochemistry and stereochemistry of 4 were established through the indicated reaction sequence and by means of n m r.



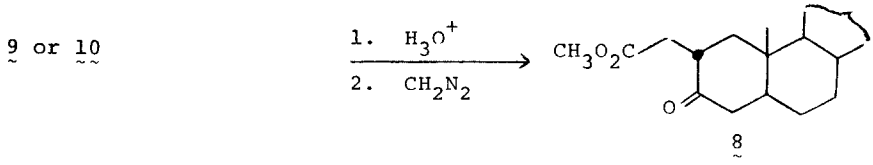
3 4 (mp 138-140°) 5 (mp 154-155°) 6 (mp 175-177°) 7 (mp 127-128°) 8 (mp 100-102°)

The reaction of 4 with sodium methoxide at room temperature or at -15° yielded a mixture of at least eight products. However, when 4 was dissolved in refluxing methanol and 3-4 equiv. of sodium methoxide was added at once, 9 and 10, in a ratio of ca. 2:1, were formed in a quantitative yield. The two products were separated by preparative thin layer chromatography and shown to be isomeric ($C_{31}H_{52}O_3$) by elemental analysis. The more reasonable alternative structures 11-13 (obtainable via an intermediate of type 2) were ruled out by the absence of enol ether or conjugated ester absorption in the ir as well as the absence of a low field nmr absorption corresponding to H_a in 13.

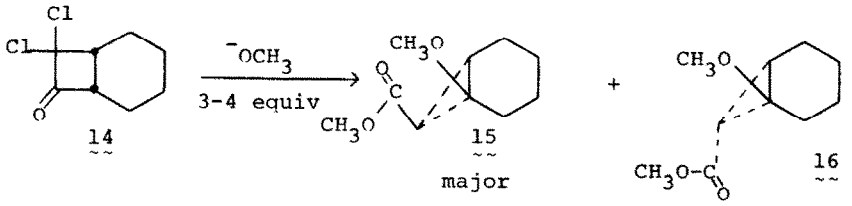




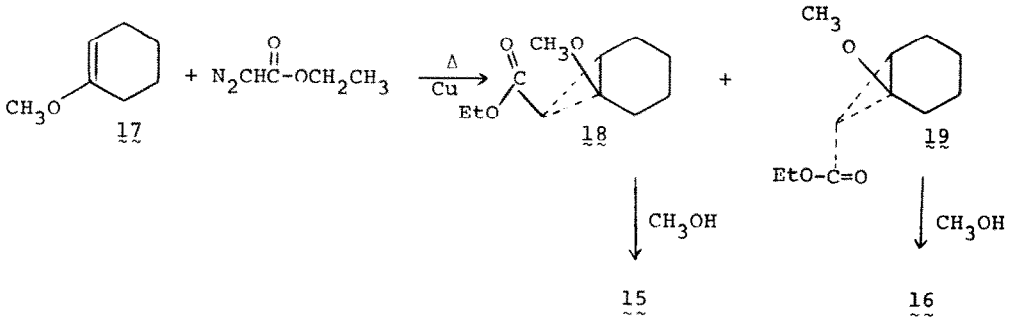
The ir and nmr spectra of 9 and 10 indicated a methyl ester and a methyl ether, in agreement with the above structures. Further structural evidence was provided by the aqueous acid ring-opening[4] of either 9 or 10 to the ketoester 8. Both isomers were stable to the reaction conditions of their formation,[5] but upon prolonged treatment with sodium methoxide of a higher concentration, 9 was slowly converted to 10.



An analogous reaction of the dichlorocyclobutanone 14,[6] gave the norcarane derivatives 15 and 16 in a ratio of ca. 20:1 as determined by gas chromatography, in 70% isolated yield. Reaction of the mixture with 2,4-dinitrophenylhydrazine reagent[4] yielded the 2,4-dinitrophenylhydrazone of cyclohexanone acetic acid methyl ester, identical with an authentic sample.



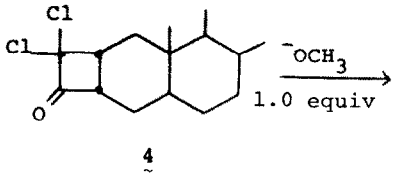
Unambiguous structure proof for 15 and 16 was provided by their synthesis from 1-methoxycyclohexene (17) as outlined below. The exo stereochemistry was assigned to the major isomer 18 since carboethoxycarbene adds to olefins with the major isomer having the least crowded arrangement of substituents.[7]



Cyclopropanes 15 from both sources were isolated and found to be identical in all respects. Methyl ester 16 prepared from 19 had the same glc retention time as the minor isomer 16 (not isolated) which was formed in the reaction of 14 with sodium methoxide. The stereochemistry indicated for the major isomers 9 and 15 has been established by methods which will be described in the full paper.

There are several mechanisms which explain the cyclopropane formation. To distinguish between the possible mechanisms, we reacted 4 with 1.0 equiv. of sodium methoxide in refluxing methanol and obtained 20 in 90% yield (mp

106-108°). The structure of 20 was established from elemental analysis and spectral data.

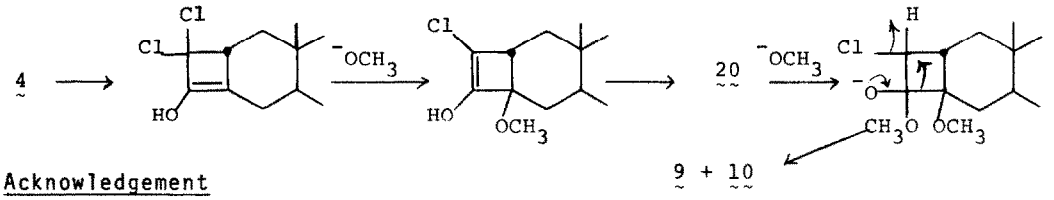


4 20

IR 1788 cm $^{-1}$ (α-chloro-cyclobutanone)

NMR 6.7τ, (s, 3H - OCH_3)
4.5τ, (d, 1H - $COCHCl$-)

Reaction of 20 with 1 equiv. of sodium methoxide in refluxing methanol gave a quantitative yield of 9 and 10 in an identical ratio as obtained from 4. The formation of 20 as an intermediate supports the following mechanism for the cyclobutane to cyclopropane conversion.[8,9]



Acknowledgement

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