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STEREOSELECTIVE OXIDATION OF CYCLOPROPENES TO ACYCLIC ENONES

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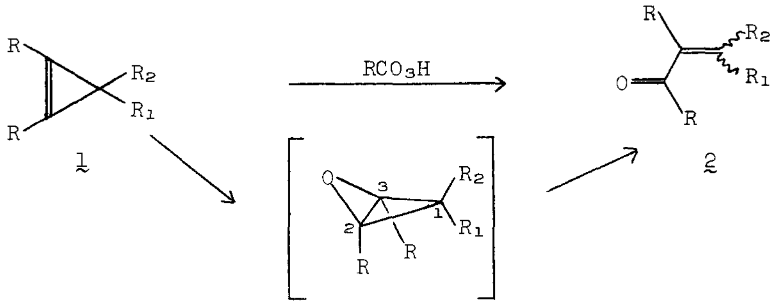
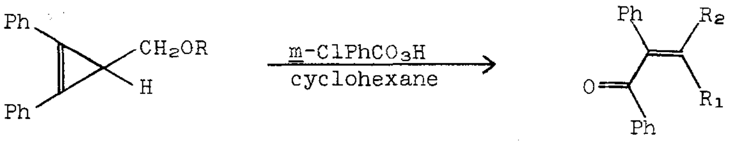
The peracid oxidation of monocyclic cyclopropenes 1 with a single substituent, R_1, in the allylic position (R_2 = H) lead to a mixture of enones 2.[1] When R_1 was carbomethoxy (R = Me, R_2 = H), the major isolated isomer of enone 2 had R_1 cis to the carbonyl group.[1a] Similarly, when R_1 was phenyl (R = Ph, R_2 = H), the kinetic yields of (Z)- and (E)-α-phenylchalcones were 81 and 19%, respectively.[1b] If oxabicyclobutanes are formed as intermediates[1,2] by epoxidation of 1, peracid attack on the cyclopropene double bond should occur mainly trans to the bulky substituent, R_1. With this knowledge about the stereochemistry of oxabicyclobutane 3, the apparently preferred mode of oxabicyclobutane rearrangement transforms exo-substituents at C-1 (R_1) into β-enone substituents located cis to the carbonyl group.



3a, R_1 = large, R_2 = small
3b, R- = small, R_2 = large

With both cyclopropenes[1a,b] studied, however, the exo substituent, R_1, of oxabicyclobutane 3 was also the more bulky substituent. An alternative explanation for the rearrangement stereochemistry of oxabicyclobutanes could be that the more bulky C-1 substituent always is placed cis to the enone carbonyl group independent of whether the more bulky substituent is endo or exo to the oxabicyclobutane ring in 3.

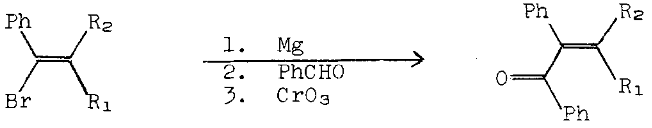
We have determined that the latter explanation is incorrect by oxidation of cyclopropenes 4 and 5 which form enones 6a-b and 7a-b. In a hydrocarbon solvent, the hydroxy group of cyclopropene 4 should complex with peracid so that oxidation of the double bond occurs cis to the more bulky methylene hydroxy group.[3a] Ether 5, however, should oxidize primarily trans to the bulky ether group.[3b] In this way both postulated oxabicyclobutanes, 3a and 3b, can be generated to test whether the size of the substituent controls the stereochemistry of the product enones.



4, R = H
5, R = Me

6a, R_1 = CH_2OH, R_2 = H
6b, R_1 = H, R_2 = CH_2OH
7a, R_1 = CH_2OMe, R_2 = H
7b, R_1 = H, R_2 = CH_2OMe

Cyclopropene 4 was synthesized as described before[4] and converted into ether 5[5] by treatment with sodium hydride and methyl iodide. Synthesis and stereochemical assignments of alcohols 6a-b are described elsewhere.[6] Methyl ethers 7a-b[5] were synthesized in a 94:6 ratio by a Grignard reaction with benzaldehyde and the isomeric bromo ethers 9a-b followed by oxidation of the resulting alcohols with CrO_3/pyridine. The bromo ethers[5] were made by sequential treatment of the known 1-bromo-1-phenylpropenes 8a-b[7] with N-bromosuccinimide and sodium methoxide.

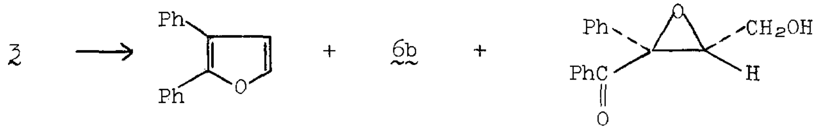


8a, R_1 = Me, R_2 = H
8b, R_1 = H, R_2 = Me
9a, R_1 = CH_2OMe, R_2 = H
9b, R_1 = H, R_2 = CH_2OMe

7a, R_1 = CH_2OMe, R_2 = H
7b, R_1 = H, R_2 = CH_2OMe

The stereochemistry of the ethers 7a-b was assigned in two ways. The Grignard reagent was independently protonated to give only (E)-cinnamyl methyl ester which suggests that addition of benzaldehyde and oxidation should primarily produce isomer 7a. Furthermore, the nmr absorption for the vinyl hydrogen and allylic hydrogens of 7a were slightly upfield from those of 7b, the same as observed for the (Z)- and (E)-stereoisomers of alcohols 6a and 6b.[6]

The isolated products of m-chloroperbenzoic acid oxidation of cyclopropene alcohol 4 in cyclohexane were:



10

11

In a separate experiment, 11[5] was the sole product of epoxidation of enone 6b. The facile dehydration of 6a to furan 10 was expected and was previously observed.[6] Epoxidation of cyclopropene ether 5 in cyclohexane gave only ethers 7a and 7b.

Quantitative analysis of product mixtures was done by repetitive nmr integration of the final worked-up mixture. The relative kinetic yields of alcohols 6a and 6b were equated to the observed yields of 10 and (6b + 11). Control analyses of synthetic mixtures of products that had been treated to the reaction conditions and workup showed an analytical accuracy of ± 2%. Starting cyclopropenes were stable in cyclohexane solutions of m-chlorobenzoic acid.

The average values for the kinetic product stereochemistries from independent runs are summarized in Table I. These values were invariant with percent conversion of peracid over the range 13-82%. Because of hydrogen bonding, alcohol 4 is expected to produce oxabicyclobutane 3b which gave predominantly enone 6b. Ether 5, on the other hand, should produce primarily oxabicyclobutane 3a and gave mainly enone 7a. In both cases, the exo substituent at C-1 in structure 3 was converted mainly to the cis-β-enone substituent (R_1 of 2) independent of the relative bulks of R_1 and R_2. This result is in agreement with Extended Hückel calculations[1b] if the enone products are generated in a transoid conformation. Even if oxabicyclobutanes are not intermediates, the results show for the first time, independent of the relative sizes of R_1 and R_2, that the C-1 substituent trans to the approach of the peracid and the cyclopropene double bond is transformed into a cis-β-enone substituent of the product.

Table I. Average Product Stereoselectivities for Oxidation of Cyclopropenes 4 and 5 in Cyclohexane.

Cyclopropene	% (Z)[a]
Alcohol 4	28.1 ± 0.7 (8)
Ether 5	67.6 ± 0.3 (2)

[a] Normalized percent of initial product with the β-enone substituent cis to the carbonyl group. Errors are standard deviations with the indicated degrees of freedom.

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