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THE ADDITION OF DICHLOROCARBENE TO METHYLENECYCLOHEXAN-4-ONE ETHYLENE ACETALS--THE ABSENCE OF SYNERGISM.

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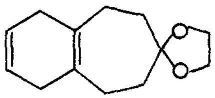
It was suggested that prior coordination of CCl_2 to an oxygen atom of ketal 1 led to a three-fold reactivity advantage of the central (relative to the peripheral) π bond.[1] This prompted a detailed study[2] of CCl_2 addition to cyclohexenes 2-5[3], which failed to uncover evidence of ketal-mediated carbene addition.[4] Nor was there cogent evidence for the intermediacy of ylidic species (6) which could efficiently transfer the Cl_2C^- fragment to activated π bonds.[2]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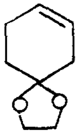
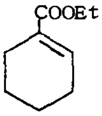
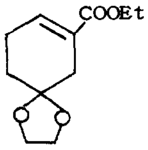

2 (0.44)


3 (0.11)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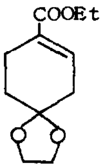
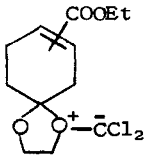

5 (0.028)


6

However, it was noted that addition-displacement sequences which passed through 6 would require front-side displacement of the Cl_2C fragment from the oxygen carrier to complete the cyclopropanation.[5] The forbidden[6] character of this step might itself have been responsible for the observed lack of synergism.

To test this possibility, we have now determined the relative reactivities of methylenecyclohexanes 7-10 (Scheme I) toward CCl_2 generated from $C_6H_5HgCCl_2Br$.[7]

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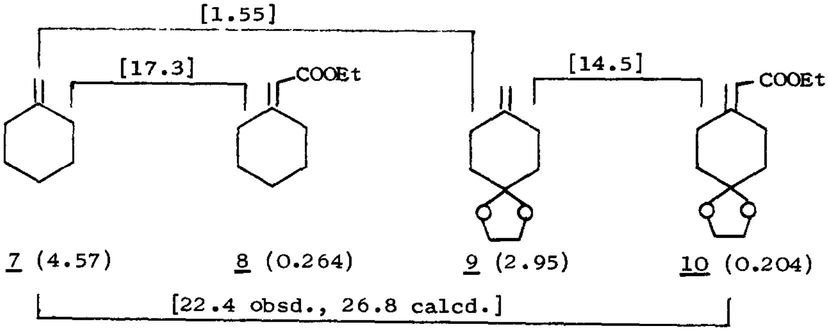
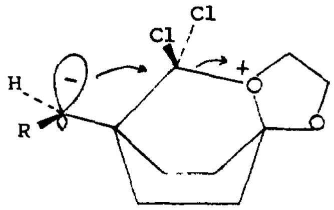
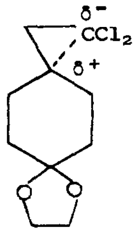
Scheme I



Dichlorocarbene addition-displacement sequences, mediated by the ketal functions of 9 or 10, would involve intermediates such as 11, in which transfer of the Cl_2C fragment can be accomplished by back-side displacement.



11 (R = H, COOEt)



9T

Olefin 8 was prepared by the procedure of Wadsworth and Emmons,[8] and 9 and 10 were derived from cyclohexane-1,4-dione monoethylene acetal[9] by application of Wittig reactions.[10,11] 1,1-Dichlorocyclopropanes were prepared from 7 and 9 with ethyl trichloroacetate and sodium methoxide,[12] and from 8 and 10 with $C_6H_5HgCCl_2Br$.[7] The new olefins (9 and 10) and the new dichlorocyclopropanes (corresponding to olefins 8-10) were each fully characterized.

The relative reactivities[13] of the olefins toward CCl_2 were determined from duplicate runs, in which each olefin was allowed to compete with cyclohexene (Cy) for an insufficiency of the carbene, generated[7] in benzene solution at 80-85°. The reactivities relative to Cy (numbers in parentheses) appear in Scheme I, which also includes relevant reactivity comparisons [numbers in brackets]. The % average deviation from the mean reactivity was less than 4% for substrates

7-9; for 10, it was 6%. Cross-check competitions[13] were performed for the pairs 7/9, 7/10, and 8/10; observed and calculated reactivities agreed to within 3% in the former two cases, and to within 8% in the latter case.

Methylenecyclohexane (7) is 4.57 times more reactive toward CCl_2 than cyclohexene, reflecting the former's ability to support partial positive charge on a tert. carbon in the unsymmetrical transition state for CCl_2 addition.[2,13] Introduction of a carboethoxy substituent (8) leads to a reactivity decrease of 17.3. Although expected, this decrease is larger than that encountered in the endocyclic series (Cy/3 = 9.1). Introduction of the 4-ethylene acetal substituent (9) decreases reactivity by 1.55, which signals an unfavorable inductive effect operating in transition state 9T; it is less than the deactivation of 2.3 observed in the endocyclic series (Cy/2).[2] No synergism is apparent.

Assuming additivity, one calculates from the individual deactivations of 8 and 9, that 10 should be 26.8 ± 1.5[14a] times less reactive than 7. Comparison of 7 and 10 to Cy (7/10) reveals a deactivation of 22.4 ± 1.5.[14b] The small difference is not significant at the 90% confidence level,[15] and should not be taken as evidence of synergistic addition to 10. Rather, the data are in accord with the additivity of substituent effects in carbene olefin addition reactions.

The results exclude the back-side attack requirement as sole cause of the lack of synergism in CCl_2 additions to olefins 2, 4, 5, 9, and 10. Why is synergism not observed? A likely reason is that oxygen competes poorly with the π bond as a center for CCl_2 addition: either the activation energy for direct addition of CCl_2 to $C{=}C$ is lower than that for addition to $-\underset{\cdot\cdot}{\ddot{O}}-$, and simple cyclopropanation occurs, or any formation of an O-ylid leads to alternative, lower-energy processes (reversion, reaction with CCl_2) in preference to the cyclopropanating addition-displacement pathway (cf., 11).[16]

It is to be noted that reactions initiated by carbenic attack on the oxygen atoms of allylic and homoallylic ethers are known for methylene (Cu carbenoid),[17] carboethoxycarbene,[18] dicarboethoxycarbene,[19] and lithium dichloromethide.[20] Such processes ought to decrease in competitive ability as carbenic reactivity decreases. Indeed, with the highly selective[13] dichlorocarbene, sulfur[21] and (to a lesser extent) nitrogen[22] atoms can compete intramolecularly with a π

bond as a site for addition, but oxygen atoms apparently cannot.[23] Relative to sulfur, this competitive failure of oxygen may be due to its intrinsically lower nucleophilicity, or to the lack of dπ-pπ stabilization and consequent (non-productive) instability of an O-ylid. This analysis suggests that the reactions of CCl_2 with sulfur analogs of 9 and 10 should be the next subject of our continuing search for synergistic dichlorocarbene additions.

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(14)(a) The probable error is based on the errors in the individual mean values which go into the calculation. (b) The extreme deviation of 3 determinations is taken as the error.
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(16) Intermediate 11 can be constructed from Dreiding models, but is rather strained if a tetrahedral oxonium center is incorporated. The strain is mitigated by substitution of a trigonal oxonium center. The correct choice is probably the latter; the inversion barrier for trialkyloxonium ions is low: J. B. Lambert and D. H. Johnson, J. Amer. Chem. Soc., **90**, 1349 (1968).
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