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NONSTEREOSPECIFICITY IN THE CYCLOADDITIONS OF KETENEIMINIUM SALTS TO OLEFINS. EVIDENCE FOR A STEPWISE MECHANISM.

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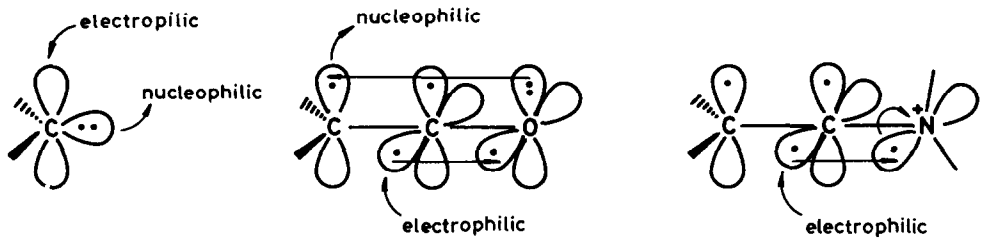
Summary: *The stereospecificity of the olefin-keteneiminium salt reaction is shown to be dependent on the nitrogen substituents. This is taken as evidence for a stepwise mechanism.*

Ketenes are exceptional reagents in their capacity to undergo concerted [2+2] cycloadditions with olefins.[1] This is a consequence of an unusual electronic structure[1,2] featuring a high-lying filled orbital with maximum coefficient at C_2 and a very low-lying empty orbital with its larger coefficient at C_1. This 1,2 dipolar[1], pull-push[1,3] or ambiphilic[4] character of ketenes enables them to initiate simultaneous bonding at C_1 and C_2 in their reactions with olefins. In these processes, the oxygen atom serves as a relay between the two orthogonal π systems (Scheme 1).

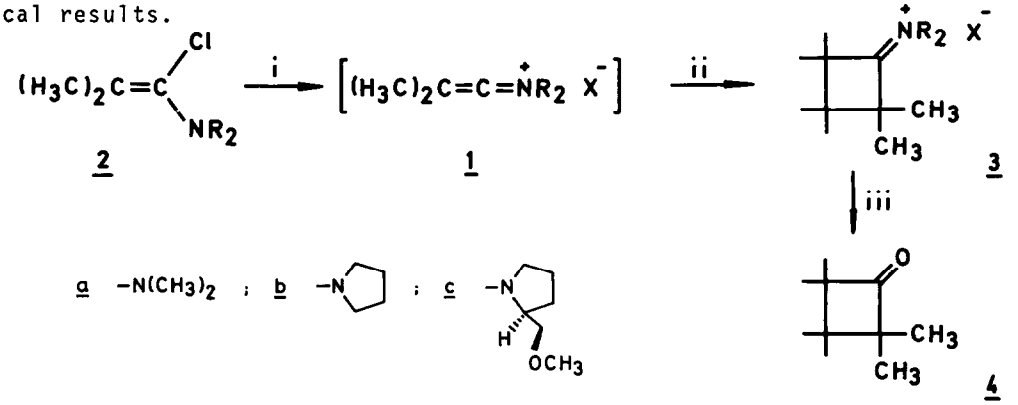


1,1 dipole **1,2 dipole** **1,2 dipole ?**

Scheme 1

This 1,2 dipolar character is obviously absent in keteneiminium salts since there is no available lone pair on the nitrogen atom ; nevertheless they readily undergo [2+2] cycloadditions.[1,5,6] Mechanistic evidence on these reactions is very sparse. Here initial bonding at C_1 is facilitated by the presence of a very low-lying $\pi^*_{C=N}$ orbital with maximum coefficient at C_1. However, bonding at C_2 should not occur before a rotation around the carbon-nitrogen bond has created a nucleophilic enamine system. It cannot be readily estimated where, on the energy profile, this rotation will take place . Yet, the rate of rotation should be influenced by the nature of the nitrogen substituents.

We have thus examined the reaction of cis-cyclooctene, cis-and trans-but-2-ene with keteneiminium salts 1a-c which differ in the nature of their nitrogen substituents (Scheme 2). Compounds 1a-c were prepared in situ from the corresponding α-chloroenamines 2 which, in turn, were synthesized by described procedures from the corresponding amides.[6,7] The cycloadditions were performed at 20°C in CH_2Cl_2 in the presence of $ZnCl_2$ (cis-cyclooctene) or $AgBF_4$ (butenes). Other Lewis acids (e.g. $TiCl_4$) can also be used without affecting the stereochemical results.



Reagents i : $AgBF_4$ or $ZnCl_2$; ii : olefin ; iii : H_2O , pH 13 (cyclooctene) or pH 1 (butenes)

Scheme 2

The results are shown in Table I. With 1a (A,D,G.), the reactions are highly stereospecific but a small amount (<10%) of the wrong isomer could be detected in the crude adducts from cis-and trans-but-2-ene. The nonstereospecific portion of the cycloadditions of cis-olefins increases in going from 1a to 1b and 1c. A substantial amount of the trans isomers is already detected in the crude adducts from cis-but-2-ene (E,F). In addition, the hydrolysis is always accompanied by a substantial cis ⟶ trans isomerization. The reaction of 1b and 1c with trans-but-2-ene is more stereospecific and less isomerization is observed on hydrolysis.

The facile isomerization of the various adducts 3 raises a question about the stereospecificity of the cycloaddition. Does the "wrong" isomer come from the cycloaddition itself or from some uncontrolled isomerization after cycloaddition ? A clearcut answer comes from the determination of the enantiomeric excesses for the cis and trans cyclobutanones formed from 1c. If the "wrong" isomer is formed by isomerization after the cycloaddition step, both cis and trans adducts should be obtained with the same enantiomeric excess. This is practically the case for the adduct to trans-but-2-ene (I). On the other hand, *with cis-olefins, the trans-isomers are formed with a much lower enantiomeric excess than the cis isomers. This clearly indicates that these cycloadditions are accompanied by a substantial loss of the original configuration of the olefins*

Table 1 : Steric Course of Cycloadditions of 1 to Olefins

	Olefins[a]	1	Crude Adducts 3 cis:trans[b]	Cyclobutanones 4 yield[c]	cis:trans[d]	ee(cis)%[e]	ee(trans)%[e]
A		1a	-	80	95:5	-	-
B	Cis-cyclooctene	1b	-	50	71:29	-	-
C		1c	-	55	78:22	94	42
D		1a	90:10	65	93:7	-	-
E	Cis-but-2-ene	1b	70:30	63	9:91	-	-
F		1c	50:50	64	13:87	64	12-16
G		1a	7:93	68	1:99	-	-
H	Trans-but-2-ene	1b	2:98	49	4:96	-	-
I		1c	0:100	52	20:80	97	94

(a) The olefins are configurationally stable in the presence of $AgBF_4$.

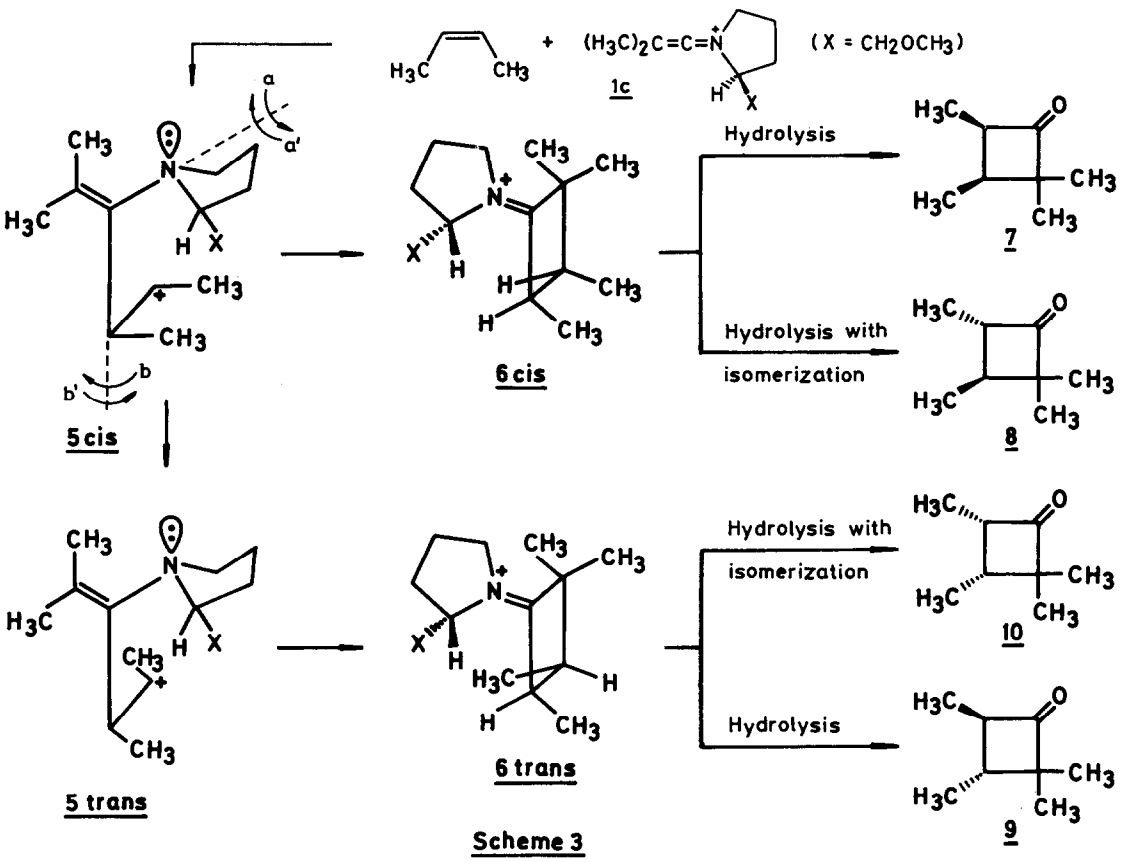
(b) With cis- and trans-butene, an estimate (± 5%) of the stereochemical composition of crude 3 could be obtained by 200 MHz NMR analysis.

(c) Fully characterised pure cyclobutanones. In addition, some amide originating from the hydrolysis of unreacted 1 was isolated.

(d) Determined by 200 MHz NMR analysis. This ratio was found to be dependent of the conditions (pH, time) of hydrolysis.

(e) Determined by 200 MHz NMR analysis in the presence of Eu $(hfc)_3$.

A possible mechanism is shown for the addition of 1c to cis-butene. A least-hindered approach of the two reactants would lead to intermediate 5 cis. Rotations a and b would create the enamine system and allow for the formation of the second bond. They appear to be a reasonable choice since (a) they produce less steric hindrance than their counterpart a' and b' (b) they lead to adduct whose absolute configuration corresponds to that found earlier for the adduct from 1c of cyclopentene. Hydrolysis of 6 leads to the cis-cyclobutanone 7 accompanied by its epimer 8 resulting form cis → trans équilibration during hydrolysis. Both 7 and 8 are expected to be formed with high ee on the basis of earlier observations[6]. Since a lower ee is observed for the trans portion of the cyclobutanone, a stereochemical leak must have occured before the formation of the second bond. This can be accounted for by isomerization of some 5- cis-to 5-trans. Cyclization would give 9, the enantiomer of 8. Since trans→cis isomerization should be less important, the contamination of 7 by its enantiomer 10 should be less important. The ee for the cis isomer should then be higher than for the trans, as found experimentally.



Scheme 3

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