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THE REGIOCHEMICAL CONSEQUENCES OF C-HAL HYPERCONJUGATION IN THE 1,3-DIPOLAR CYCLOADDITIONS OF NITRILE OXIDES[1]

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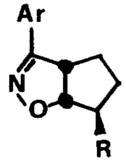
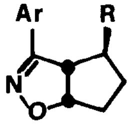
In a previous letter[2] we have shown that the polar and steric effects on the regioselectivity of the 1,3-dipolar cycloadditions of benzonitriloxide (BNO) could be separated and evaluated by using as dipolarophiles the 3-substituted cyclopentenes. Since their envelope conformations ensure the same steric environments for both the regioisomeric attacks <u>anti</u> to the substituent, the polar effect on the regioselectivity could be easily recognized, the regioisomer I being favoured by electron-releasing substituents (R=alkyl) and regioisomer II being predominant with electron-attracting substituents (R=Ph,NMe_2,OH,OCH_3,$OCOCH_3$). The results fitted the frontier orbital approach[3] well, and the free energy differences $\Delta\Delta G_p^{\neq}$ between the two regioisomeric pathways was found to correlate roughly with Taft's polar substituent parameters.

I



II



We wish now to report and discuss the special features observed in the 1,3-dipolar cycloaddition of nitrile oxides to 3-chloro and 3-bromo cyclopentene.

Admixture of BNO or mesitonitrile oxide in ether or benzene with 3 equivs of the 3-halocyclopentene afforded the two <u>anti</u> regioisomers I and II, which were separated by colunmn chromatography with a total yield over 90%[4]. The regiochemical assignment was firmly established by independent syntheses from the corresponding alcohols[2] and the stereochemical assignment relies on the low values ($<$ 0.5Hz) of the coupling constants between the cyclopentane proton on the carbon bearing the halogen and the adjacent bridgehead proton. The isomer distribution was measured by glc analysis on an OV 17 column, by comparison with mixtures of known composition.

Surprisingly, as shown in Table 1, in none of the cases investigated so far do the expected

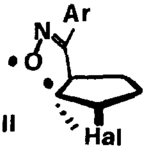
TABLE 1. Distribution of the anti regioisomers in the reaction mixtures

Ar	R	Solvent, °C	Isomer distribution[a] I	II	Ratio I/II	$\Delta\Delta G_p^{\neq b}$
Ph	Cl	ether, 0[c]	55	45	1.22	0.11
		benzene, 25	50	50	1.00	0.00
Ph	Br	ether, 0[c]	67	33	2.03	0.38
		benzene, 25	64	36	1.78	0.34
Mesityl	Cl	benzene, 25	50	50	1.00	0.00
Mesityl	Br	benzene, 25	65	35	1.86	0.36

[a] Percentage of the total mixture of anti 4- and 6-halo tetrahydrocyclopent [d] isoxazoles. [b] kcal/mole. [c] The isomer distribution does not change appreciably at 25° or in the presence of excess trietylamine.

cycloadducts of type II predominate, in spite of the strong electron-attracting power of the halogens. In the case of 3-bromocyclopentene, cycloadducts of type I prevail, whereas the cycloadditions to 3-chlorocyclopentene are rather unselective.

A somewhat naive rationalization of this unusual behaviour would be the intervention of a Firestone's diradical III[5], anchimerically assisted by the halogen. The β-halogen assistance in radicals is now well-documented from Skell's work on radical halogenation[6] and from epr investigations[7]. However, the small difference (0.35 kcal/mole, see Table 1) between the regiochemical effect of Br and Cl is not reconcilable with the reported[6a,b] far larger bridging ability of Br with respect to Cl. On this ground, as well as on the general unlikelyhood[8] of the diradical hypothesis,we looked for an alternative explanation in the light of the recent applications of perturbation theory to cycloadditions.[3]

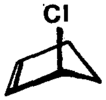


III

We have performed a CNDO/2 calculation on the pseudoaxial and pseudoequatorial conformers of 3-chlorocyclopentene[9]. The latter conformer is found to be slightly favored over the former by 0.155 kcal/mole. The relevant data for both conformations are quite similar and are reported in Table 2.[10]

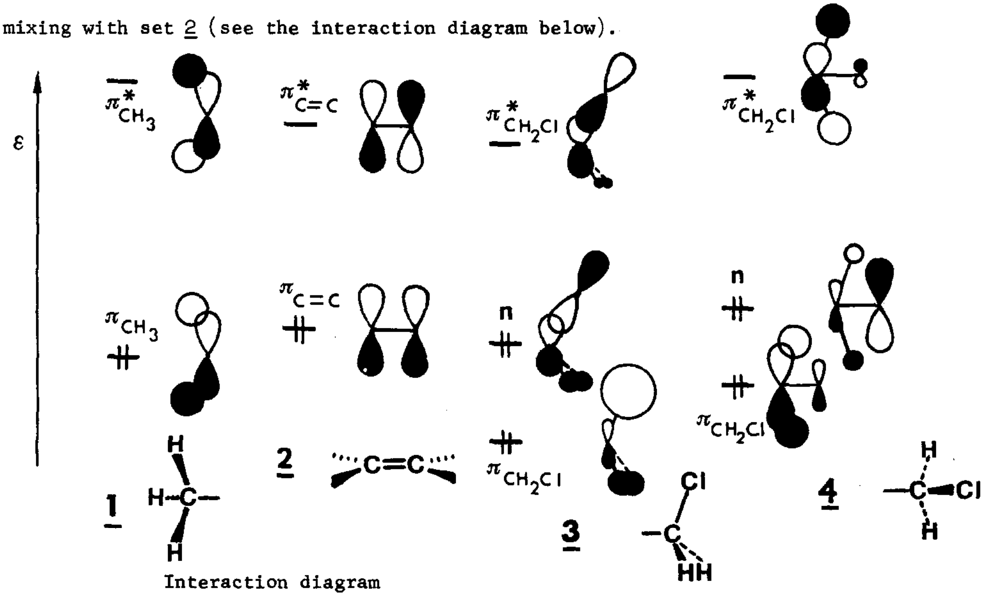
The simple inductive model-which correctly accounts for our previous results[2]-predicts the larger coefficients to be on C_2 for the π and on C_1 for the π^* orbital. However, the CNDO/2 calculations show that the coefficients on the two carbon atoms are practically equal, and indeed slightly larger on C_1 in π and on C_2 in π^*. Under these circumstances the interaction diagram for the nitrile oxides cycloadditions[2,3b,c] predicts only a slight preference for regio-

TABLE 2. CNDO/2 eigenvalues and eigenvectors for the π orbitals of 3-chlorocyclopentene

						
	C_1	C_2	ε(ev)	C_1	C_2	ε(ev)
Eigenvectors, π*	0.522	-0.574	4.68	0.577	-0.583	4.39
π	0.474	0.458	-12.70	0.474	0.461	-12.80
π charge	0.011	-0.024		0.012	-0.019	
Total charge	0.000	-0.008		-0.005	-0.005	
μ, D	2.08			2.35		
Total energy (a. u.)	-57.123487			-57.123734		

isomer I, in fair agreement with the experimental results.

The origin of the effect of an allylic chlorine on the π orbital coefficients could be deduced by an analysis of the CNDO/2 wave functions of 3-chlorocyclopentene and of the related crotyl chloride as a suitable model, with the aid of the "cut off" procedure, a versatile orbital decoupling technique[11]. A simplified account is given here for two limiting arrangements of CH_2Cl in crotyl chloride, in which the C-Cl bond eclipses the p_z orbitals (A) or lies in the p_z nodal plane (B). By interrupting the conjugation between the p_z orbitals of the double bond and all the AO's of the methyl and CH_2Cl groups we obtained the set of the localized orbitals of the double bond 2 and those of CH_3 (1)[12] and CH_2Cl (3 for A, 4 for B), which are capable of mixing with set 2 (see the interaction diagram below).



Interaction diagram

The lower and upper orbitals of sets 3 and 4 are identifiable as the π_{CH_2Cl} orbitals[13], whereas the middle orbital has mainly n character but has acquired a sizable p_z coefficient at the carbon atom by mixing with the former. As it may be seen there is a strong interaction between $\pi_{C=C}$ and n because of their close energies. This hyperconjugative interaction, together with the analogous one of the π_{CH_2Cl} orbital, polarizes the double bond toward the C-atom adjacent to the CH_3 group[14,15] and their combined action more than compensates the opposite effect of the methyl.[16]

Our regiochemical results indicate that the -CHBr- hyperconjugation is even higher, this in good agreement with what has been recently observed in PE spectra of allyl and benzyl halides.[17]

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References and Footnotes

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15. In case B the n perturber[14a] lies above the π orbital. A linear combination of the localized orbitals[14b] shows indeed that π_{CH_3} and π_{CH_2Cl} actually push the π level above n.
16. The relative magnitudes of π^* coefficients can be similarly accounted for. When the chlorine lies in the p_z nodal plane (case B), however, both the full calculation and the perturbation formalism[14] show a slightly greater π^* coefficient at the carbon atom adjacent to the CH_3 group.
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