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REGIOCHEMICAL CONTROL IN THE ALLYLIC HYDROGEN ABSTRACTION FROM 1-X-SUBSTITUTED CYCLOHEXENES.

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Allylic hydrogen abstraction is strongly affected by substituents attached to the double bond. Evidence regarding this regiochemical control is presented for the first time.

The influence of substituents in determining the hydrogen abstraction from an organic molecule has long been studied for almost all classes of organic compounds[1].

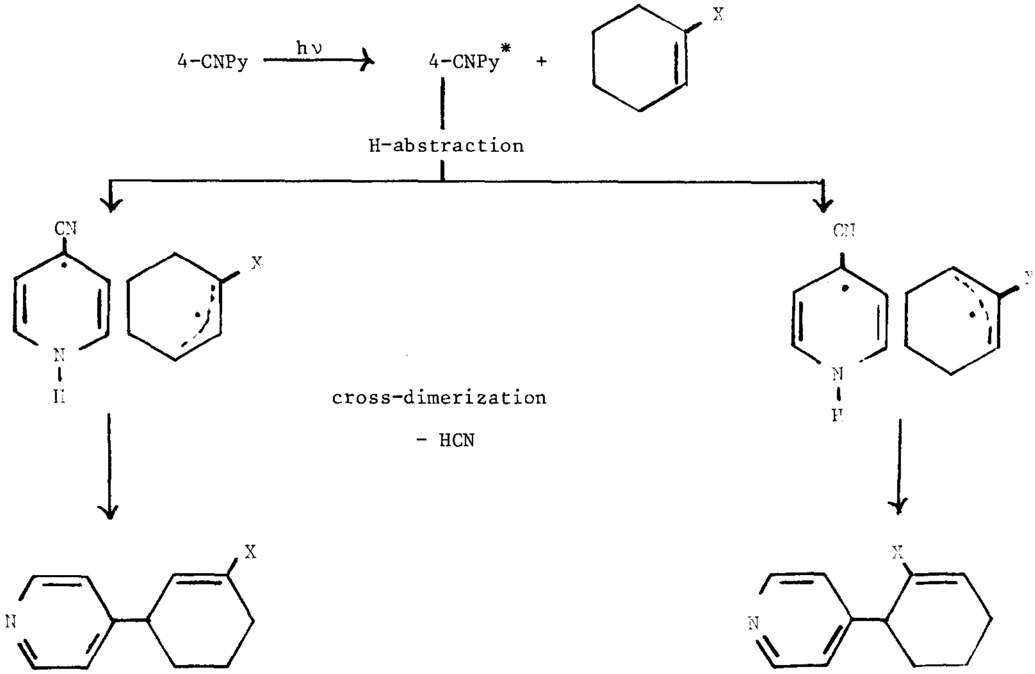
However, very little is known about the regioselectivity of the allylic hydrogen abstraction when the substituent is attached to the double bond. Allylic hydrogen abstraction occurs, for example, when an alkene reacts with N-bromosuccinimide[2a-b], t-butylhypochlorite[3], t-butylperesters[4a-b], or singlet oxygen[5]. All papers and reviews on this subject are more concerned with the mechanism of the reactions rather than with the influence of different substituents; moreover, authors have tried to semplify the product analysis by using terminal or alkyl substituted alkenes. Only in a few cases have 1-X-substituted alkenes been used[4b-6] but in these cases product analysis was not complete.

For these reasons, we started the present study with the aim of determining the selectivity, if any, involved in the abstraction of allylic hydrogen and for this purpose we chose 1-X-substituted cyclohexenes as the model molecule.

In a previous paper[7], we reported that 4-cyanopyridine (4-CNPy) when photochemically excited is able to abstract allylic hydrogens and the resulting radicals give rise to cross-dimerization with rearomatization; this reaction proved to be suitable to gain insight into the selectivity of allylic hydrogen abstraction from 1-X-cyclohexenes, see scheme 1.

In a typical experiment 1 mmole of 4-CNPy was dissolved in 20 mL of anhydrous CH_3CN 5 mmole of the cyclohexene derivative was added and the resulting solution irradiated in a quartz vessel at 254 nm in a RPR-100 Rayonet reactor. The reaction time was 14 h for the preparative reactions and 1 h for determining the relative rate of allylic hydrogen abstraction; in this last case, the reactions were run all together in a merry-go-round apparatus. At the end of the irradiation time, a standard was added and the mixture examined by gas-chromatography.

SCHEME 1



	3 allylic derivative	6 allylic derivative
X=OCH_3	1	2
X=$OCOCH_3$	3	4
X=H	5	
X=$COCH_3$		6
X=CN		7
X=Cl[a]	8	9

[a] see ref. 8

The results are summarized in table 1

TABLE 1[a]

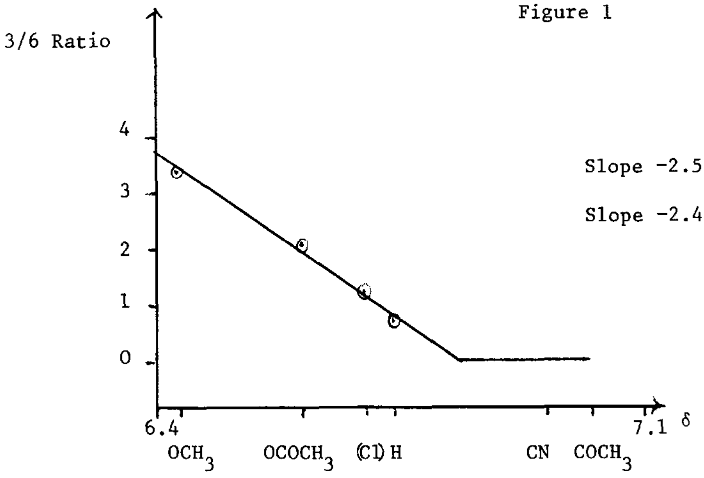
	3 derivative	6 derivative	3/6 ratio
OCH_3	$16.6\ 10^{-2}$	$4.7\ 10^{-2}$	3.54
$OCOCH_3$	$8.4\ 10^{-2}$	$4.2\ 10^{-2}$	1.99
H	$9.7\ 10^{-2}$[b]		1
$COCH_3$	0	$1.2\ 10^{-2}$	----
CN	0	$0.8\ 10^{-2}$	----
(Cl)			(0.67)

a mmole of products

b Statistically corrected

As can be seen, the substituent influences the hydrogen abstraction from position 3 to a greater extent than from 6. The abstracting species (i.e. the nitrogen radical in the photoexcited pyridine [9] ) which is electrophylic in character seems to be very sensitive to the charge density induced by the substituent on the double bond. A group with a mesomeric electron donating effect such as OCH_3 or $OCOCH_3$ apparently increases the electron density on position 3 more than on position 6. Electron withdrawing groups, like $COCH_3$ or CN, show the reverse effects so that position 3 becomes completely unreactive. We were unable to find a linear free energy relationship[10] with the σ values at either position but it seems interesting to emphasize that a correlation between the 3/6 ratio and the NMR chemical shift of the vinylic proton in the starting cyclohexenes has been obtained[11]. (Figure 1)

Figure 1



Slope −2.54, r=0.993 without Cl

Slope −2.43, r=0.992 with Cl

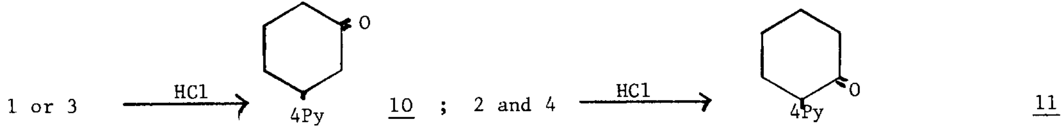
Since the chemical shift reflects the electronic situation of the molecule, this correlation is a support for our conclusions.

To our knowledge, selectivity of this type in hydrogen abstraction has never been reported in the literature: along this line, further work is in progress using photochemically induced reactions with 1-X-substituted cyclohexenes carring other substituents. Because heterocyclic bases, when excited, may give rise to exciplexes owing to different reactions pathways, non photochemical radical sources should to be checked in order to test the generality of the selectivity observed.

Spectral data

In the case in which $X=OCH_3$ and $OCOCH_3$, the reactions products were thermally unstable, so we chose, at the end of the reaction, to hydrolize them to the corresponding ketones with diluted HCl. (Scheme 2). Separation of 1 and 2 was achieved with a Waters Liquiprep instrument using a Prepac $500/C_{18}$ column and CH_3CN as solvent. Products 3 and 4 were isolated as mixtures, hydrolized and identified as 10 and 11.

Scheme 2



1	mass frag. 189,188,174,161;	NMR 8.5 and 7.2 Py, 4.61 -CH=CX-, 3.48 CHPy, 3.55 OCH$_3$, 3.3-1.2 (CH_2)
2	189,188,174,130	8.5 and 7.1 Py, 4.95 -CH=CX-, 3.48 CHPy, 3.48 OCH$_3$, 2.3-1.2 $(CH_2)_3$
6	201,200,183,149	8.5 and 7.0 Py, 7.21 -CH=CX-, 3.9 CHPy, 2.23 COCH$_3$, 2.2-1.5 $(CH_2)_3$
7	184,169,155,144	8.6 and 7.2 Py, 6.9 -CH=CX-, 3.6 CHPy, 2.5-1.5 $(CH_2)_3$
10	175,146,132,118	8.5 and 7.1 Py; 3.0 CHPy, 2.5 CH_2-CO-CH_2, 1.9 $(CH_2)_2$

Products 5[7] and 11[13] were reported in literature; NMR: δ are quoted in ppm from TMS as internal standard; solvent $CDCl_3$. Satisfactory analytical data were reported for all new compounds.

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10 A plot of log(mmole-X/mmole-H) against σ_p for the 3 derivatives (3 points) was linear ρ= -0.49 R=0.934. No one was found for the 6 derivatives. Probably σ_{ortho} were to be used, but the reported value are not reliable.

11 We are aware that the vinylic proton when X=COCH$_3$ is shifted downfield because of the anisotropy of the carbonyl group. Theoretical calculations[12] permit the evaluation of this effect as a maximum of 0.4 δ, this brings the NMR shift to a limiting value of 6.5δ but the change did not influence the reported correlation.

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