Nucleophilic Substitution of Hydrogen in Electrophilic Alkenes[1]

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Carbanions containing leaving groups replace hydrogen in electrophilic alkenes via an addition–base induced β-elimination pathway.

We have recently reported numerous examples of the nucleophilic substitution of hydrogen in nitroarenes and electrophilic aromatic heterocycles.[2,3] The reaction proceeds via addition of the carbanion $\overline{R C}XY$ (X = leaving group, Y = carbanion stabilizing group) to the nitroarene ring, resulting in the formation of a short lived anionic σ-complex, followed by base induced β-elimination of HX from the complex to give the anion of the product, Scheme 1.[4]

Here we present a study of the nucleophilic substitution of hydrogen in aliphatic systems, i.e. electrophilic alkenes, which proceeds according to a similar mechanism, Scheme 2. Reactions of carbanions with electrophilic alkenes give, as a rule, products of Michael addition. When the carbanions contain leaving groups which can be replaced in an S_N2 type process cyclopropane derivatives are usually formed. So the main differences between aromatic and aliphatic systems are that in the former case the concentration of the adduct (σ-complex) is usually very low (the addition equilibrium is shifted to the left), the tendency to the intramolecular S_N2 type reaction of the σ-complex is negligible, and the elimination of HX to form a highly conjugated quinoid system is strongly favoured, whereas in the aliphatic systems the concentration of the adduct is high and the cyclization usually occurs readily.

One can therefore suppose that the elimination of HX from (3) will dominate over cyclization when: (a) substituent X is reluctant towards S_N2 substitution but can be eliminated as HX via an E2 or E1cb process; (b) substituents Z and R^1 provide high stabilization, hence low nucleophilicity, of
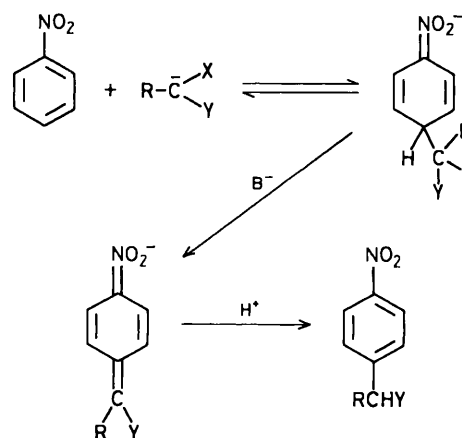
Scheme 1
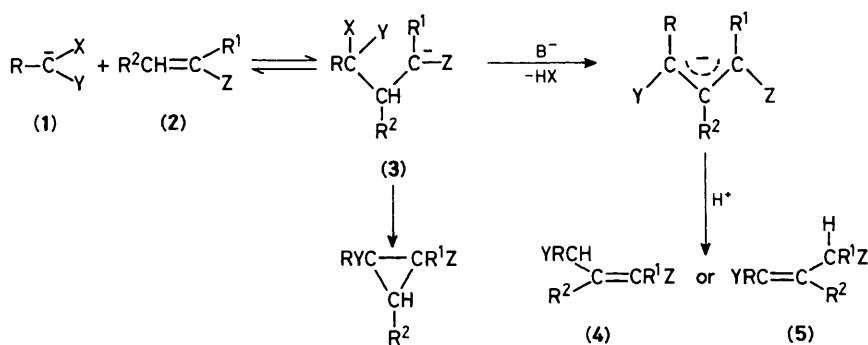
Scheme 2

Table 1. Yield of products[a] from nucleophilic substitution of hydrogen in electrophilic alkenes (Scheme 2).

R	X	Y	R^1	R^2	Z	Product (% yield)
H	Cl	SO$_2$Ph	H	Ph	NO$_2$	(4a) (55)
H	Cl	SO$_2$Ph	CN	Ph	CO$_2$Me	(4b) (65)
Me	Cl	SO$_2$Ph	H	CO$_2$Et	CO$_2$Et	(4c) (54)
Pr^i	Cl	CN	H	Ph	NO$_2$	(5a) (61) (E and Z)
Ph	OMe	CN	H	Ph	NO$_2$	(5b) (41)
H	Cl	COPh	H	Ph	NO$_2$	(5c) (40)
Cl	Cl	Cl	H	Ph	NO$_2$	(5d) (55)

[a] The n.m.r. and i.r. spectra were consistent with assigned structures; satisfactory microanalyses were obtained.

carbanion (3); (c) substituent R^2 facilitates abstraction of a geminal proton; (d) the system contains an excess of base. Indeed when all or even some of these requirements are met elimination of HX from (3) rather than cyclization occurs giving an allylic carbanion which upon protonation can give two isomeric alkenes (4) and (5).[5]

For example, chloromethyl phenyl sulphone reacts with ω-nitrostyrene and methyl 2-cyano-3-phenylacrylate giving products (4a) and (4b) respectively (Table 1). When the alkene contains only one ethoxycarbonyl group stabilizing the intermediate anion (3) (Z = CO$_2$Et, R^1 = H), strong activation of the β-hydrogen atom (R^2 = CO$_2$Et) is necessary for the reaction to occur.

Some other carbanions in the reaction with ω-nitrostyrene gave mainly products of type (5). Both the strong withdrawing character of the nitro group and activation of the β-hydrogen atom (R^2 = Ph) in the ω-nitrostyrene molecule favour the replacement of hydrogen even when the elimination of HX is rather difficult (X = OMe) and also when the leaving group is very prone to nucleophilic substitution (X = Cl α to the cyano or carbonyl group).

The reactions were carried out in tetrahydrofuran using Bu^{t}OK for the generation of the carbanions and the β-elimination. The addition step to form (3) was usually completed at −70 °C whereas the elimination of HX from (3) required a higher temperature (−50 °C—room temp. depending on the case). These observations show that elimination is the slower, rate determining step of the whole process.

References

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