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NUCLEOPHILIC SUBSTITUTION AND ELIMINATION REACTIONS ON NITROGEN ATOM

REACTION OF N,N-DIBENZYL-O-p-NITROBENZOYLHYDROXYLAMINE WITH VARIOUS NUCLEOPHILES IN DIPOLAR APROTIC SOLVENT

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The reactions of N,N-dibenzyl-O-p-nitrobenzoylhydroxylamine (DNH) with nucleophiles were found to give benzaldehyde, benzylamine and p-nitrobenzoate ion in good yields, respectively. It has been suggested that these reactions would proceed via E2 mechanism on the nitrogen atom on the basis of kinetic isotope experiment. Furthermore, S_N2 mechanism on the nitrogen atom has been inferred for the reaction of DNH with cyanide ion.

The nucleophilic substitution reaction on carbon atom has been extensively studied in the past and well understood.(1) However, no systematic study concerning the nature of nucleophilic substitution on the trivalent nitrogen atom has been attempted, though there have been some investigations on the nucleophilic substitution at oxygen atom.(2) A careful literature survey reveals that there are a few reactions which appear to be the nucleophilic substitution on the nitrogen atom.(3,4,5,6) No kinetic study, however, has been made as to elucidate the mechanism. Similarly, there has been no systematic study on the elimination reaction on the nitrogen atom.

Thus, we have prepared N,N-dibenzyl-O-p-nitrobenzoylhydroxylamine (abbreviated hereafter as DNH), m.p., 108-109°C, as a model compound to study the nucleophilic substitution and the related reactions on the nitrogen atom.

The reaction of DNH with charged nucleophiles in dimethyl sulfoxide (DMSO) gave benzaldehyde, benzylamine and p-nitrobenzoate ion, respectively, in good yields as indicated in the Table.[7)] There are two mechanisms conceivable to explain the product distribution. Although the formation of benzaldehyde could be interpreted as a modification of the Kornblum reaction,[8)] this mechanism may be ruled out since benzaldehyde was also obtained (85% yield) when DMF was used as the solvent.

Table. Product Analysis of the Reaction of DNH with Nucleophiles in DMSO at Room Temperature.[a)]

M-Nu	Reaction Time (hr.)	Product and Yield (%)				
		DNH (recov.)	PhCHO	$PhCH_2NH_2$	$p\text{-}NO_2C_6H_4CO_2M$	Others
NaN_3	24	0	76	73	quant.	----
LiCl	25	0	70	67	72	----
NaBr	24	78	19	18	22	----
NaI	50	67	24	28	33	----
NaOH	26	0	22	20	70	$PhCH_2N{=}CHPh$ 51
NaCN	35	0	8	8	quant.	$(PhCH_2)_2N\text{-}CN$ 46

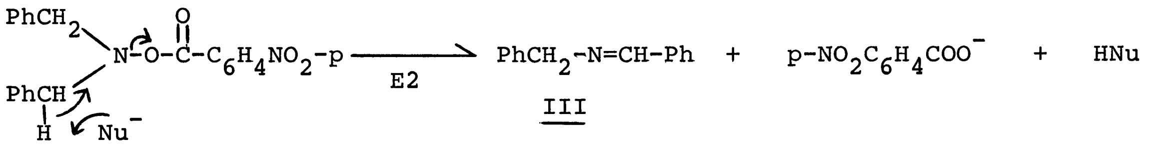
a) Small excess amount of the nucleophile was allowed to react with DNH.

Formation of benzaldehyde and benzylamine can be explained by assuming the imine III as the precursor of which intermediacy was confirmed by direct hydrolysis of the authentic imine III in the presence of HCl in DMSO. Moreover, imine III was actually isolated from the reaction with NaOH as the nucleophile.

On the other hand, there are two conceivable processes to give the imine III. The one is the base-catalyzed elimination of the carboxylate from the starting material (Path A) and the other, the decomposition of the initial product I, which was formed by the substitution on the trivalent nitrogen atom of DNH, due to the instability of the N-Nu bond and the high reactivity of the nitrenium ion II.[9)] (Path B). The latter process seems to fit nicely at least for the reaction with cyanide ion where the substitution product I was actually isolated in a substantial yield.[10)]

In order to make a choice between the two mechanisms, hydrogen-deuterium kinetic isotope effect was measured using the substrate which was labeled with D at

Path A



DNH

Path B

$$\underline{\mathrm{DNH}} \xrightarrow[\text{N-attack}]{\mathrm{Nu}^-} \underset{\underline{\mathrm{I}}}{(\mathrm{PhCH_2})_2\mathrm{N{-}Nu}} + p\text{-}\mathrm{NO_2C_6H_4COO^-}$$

$$\underline{\mathrm{I}} \longrightarrow \underset{\underline{\mathrm{II}}}{(\mathrm{PhCH_2})_2\mathrm{N^+}} + \mathrm{Nu^-} \longrightarrow \underset{\underline{\mathrm{III}}}{\mathrm{PhCH_2{-}N{=}CH{-}Ph}} + \mathrm{HNu}$$

$$\underline{\mathrm{III}} \xrightarrow[\mathrm{H_2O\ in\ DMSO}]{\text{hyd.}} \mathrm{PhCHO} + \mathrm{PhCH_2NH_2}$$

the benzylic position.[11)] The pseudo-first order rate of the reaction was measured by following the increasing amount of p-nitrobenzoate ion with a large excess of the nucleophile at 30°C. The isotope effect, thus obtained, are 7.6 and 8.1 for the reactions with N_3^- and Cl^- as the nucleophiles, respectively.

These results clearly indicate that these reactions are the base-catalyzed elimination (Path A) except for the reaction with cyanide ion. The order of the reactivities of the halide ions, $Cl^- > Br^- > I^-$, deduced from the recovered amount of the starting material and the reaction time, also support that the reaction involves the rate-determining proton abstraction by the base.

The detailed accounts of these reactions, including the course of the reaction and the nature of the nucleophile and the reaction condition, are now being investigated in these laboratories.

References and Remarks

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10) Oily liquid ; i.r. (neat) 2230 cm^{-1} (ν_{CN}) ; n.m.r. ($CDCl_3$) 6.25τ(4H, s) 2.10 - 3.10τ(10H, m). N,N-Dibenzylcyanamine is stable at room temperature, but upon distillation at 140 - 160°C under reduced pressure, it decomposed to afford N,N-dibenzylamine.

11) The deuterium content of the N,N-dibenzyl-α-d_4-O-p-nitrobenzoylhydroxylamine is found to be 100 % on the basis of n.m.r. spectroscopy and kinetic isotope experiment was carried out in DMSO by means of u.v. technique.

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