Elimination and Nucleophilic Substitution on Nitrogen Atom. Reactions of *O*-Aroyl-*N*,*N*-di(*p*-substituted benzyl)- and *O*-Aroyl-*N*-benzoyl-*N*-benzylhydroxylamines with Various Nucleophiles in Dipolar Aprotic Solvents[1)]

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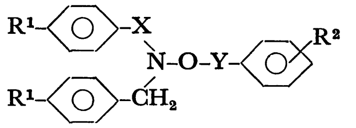
The reactions of the title compounds with various nucleophiles were found to proceed through either elimination or nucleophilic substitution on the nitrogen atom depending on both the structure of the substrate and the nature of nucleophiles used. The effect of substituent and the primary isotope effect (k_H/k_D of 7.6 and 8.1 with NaN_3 and LiCl at 30 °C) on the elimination of *O*-(*p*-nitrobenzoyl)-*N*,*N*-dibenzylhydroxylamine revealed that the reaction is an E2 process involving the rate-determining proton abstraction by base and proceeds *via* an ionic transition state of an ideal concerted type. Nucleophilic substitution on the trivalent nitrogen atom has been inferred for the reactions with such nucleophiles as diethyl sulfide, *p*-toluenethiol and sodium cyanide on the basis of product distribution.

The nucleophilic substitution and elimination reactions on carbon atom have been studied extensively in the past and well understood.[2)] However, no systematic study concerning the nature of both nucleophilic substitution and elimination reactions on the trivalent nitrogen atom has been attempted, though there have been some investigations on the nucleophilic substitution[3)] and elimination[4)] reactions at oxygen atom. A careful literature survery reveals that there are a few reactions which appear to be the nucleophilic substitution[5)] and elimination[6)] reactions on the nitrogen atom. Very recently, the occurrence of S_N2 type reaction on nitrogen atom has been well confirmed on the basis of both detailed kinetic study and product analysis by us[7b)] and Krueges *et al.*[7a)] However, as to the elimination reaction on the trivalent nitrogen atom giving either C–N double bond or C–N triple bond, a more critical examination would be necessary.

Thus, we have prepared *O*-aroyl-*N*,*N*-di(*p*-substituted benzyl)- and *O*-aroyl-*N*-benzoyl-*N*-benzylhydroxylamines as model compounds, and allowed them to react with various nucleophiles in dipolar aprotic solvents for studying both nucleophilic substitution and elimination reactions on the nitrogen atom.



(I)

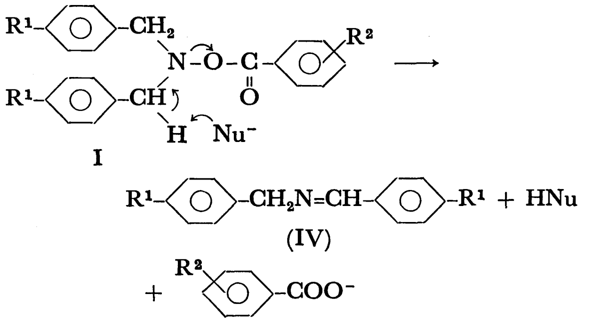
$R^1=CH_3$, H, Cl
$R^2=3,5\text{-}(NO_2)_2$, $p\text{-}(NO_2)_2$, *p*-Cl, $p\text{-}OCH_3$, $2,4,6\text{-}(CH_3)_3$
$X=CH_2$, CO $Y=CO$, SO_2

Results and Discussion

Reactions of (I) ($X=CH_2$; $Y=CO$; $R^1=CH_3$, H, Cl; $R^2=$p-NO_2, $3,5\text{-}(NO_2)_2$) with Charged Nucleophiles. The reactions of (I) with charged nucleophiles in dimethyl sulfoxide (DMSO) gave substituted benzaldehydes, substitutted benzylamines and substituted benzoate ions in good yields respectively, as indicated in Table 1. There are two conceivable mechanisms to explain the product distribution. Although the formation of substituted benzaldehydes could be interpreted as a modification of the Kornblum reaction,[8)] this mechanism may be ruled out since benzaldehyde ($R^1=H$) was also obtained (85% yield) when *N*,*N*-dimethylformamide (DMF) was used as a solvent. Formation of the aldehyde and the amine can be explained by assuming the imine (IV) as the precursor of which intermediacy was confirmed by direct hydrolysis of the authentic imine (IV) in the presence of HCl in DMSO.

Moreover, the imine (IV, $R^1=H$) was actually isolated from the reaction with NaOH as a nucleophile probably because of lower acidity of HNu (Nu=OH) than other HNu ($Nu=N_3$, Cl, I). Interestingly, the

Path A



Path B

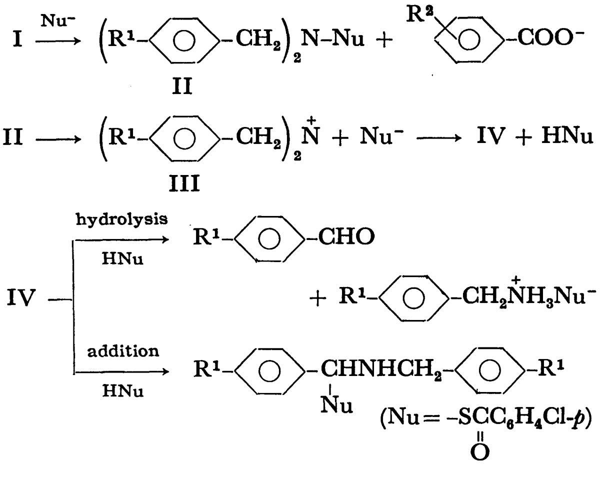
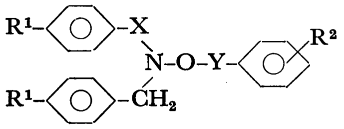
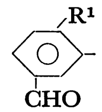
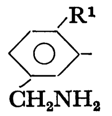
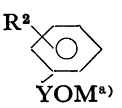
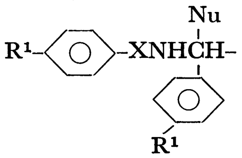
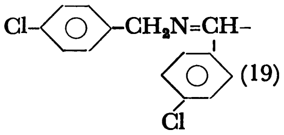
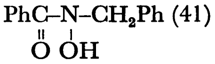
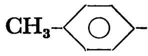


TABLE 1. THE PRODUCTS OF THE REACTION OF  WITH NUCLEOPHILES IN DMSO AT ROOM TEMPERATURE

R^1	X	Y	R^2	Nu or M-Nu	Time (hr)	Re-cov.	Producst (% Yield)				Others
											
H	CH_2	CO	p-NO_2	NaN_3	24	—	76	73	quant.	—	—
H	CH_2	CO	p-NO_2	LiCl	25	—	70	67	72	—	—
H	CH_2	CO	p-NO_2	NaBr	24	78	19	18	22	—	—
H	CH_2	CO	p-NO_2	NaI	50	67	24	28	33	—	—
H	CH_2	CO	p-NO_2	NaOH	26	—	22	20	70	—	$PhCH_2N=CHPh$(51)
H	CH_2	CO	p-NO_2	NaSC(=O)-C_6H_4Cl-p	40	—	57	29	58	35	—
H	CH_2	CO	3,5-$(NO_2)_2$	NaN_3	15	—	75	68	75	—	—
H	CH_2	CO	p-OCH_3	NaN_3	36	63	20	18	18	—	—
CH_3	CH_2	CO	p-NO_2	NaN_3	15	—	82	75	80	—	—
Cl	CH_2	CO	p-NO_2	NaN_3	20	—	64	60	76	—	
H	CH_2	CO	p-NO_2	NaCN	15	—	7	8	87	22	$(PhCH_2)_2NH$ (58)
H	CH_2	CO	3,5-$(NO_2)_2$	NaCN	15	—	25	20	small amount	—	—
H	CO	CO	p-NO_2	NaCN	15	—	—	—	27	58	—
H	CO	CO	p-NO_2	NaCN[b)]	10	—	—	—	82	39	 $\mathrm{PhC(=O){-}N(OH){-}CH_2Ph}$ (41)
H	CO	SO_2	2,4,6-$(CH_3)_3$	NaCN	20	—	—	—	72[c)]	65	—
H	CH_2	CO	p-NO_2	$(C_2H_5)_2S$	48	28	49	33	38	—	—
H	CH_2	CO	3,5-$(NO_2)_2$	$(C_2H_5)_2S$	36	13	66	62	46	—	—
H	CH_2	CO	p-NO_2	p-$CH_3C_6H_4SH$[b)]	25	13	51	40	52	—	 (31), $(p\text{-}CH_3C_6H_4S)_2$ (46)
H	CH_2	CO	p-Cl	NaCN	20	—	8	d)	72	79	—
H	CH_2	CO	p-OCH_3	NaCN	20	—	8	d)	87	65	—
H	CH_2	CO	p-OCH_3	KCN[b)]	15	53	trace	d)	30	22	—

a) as carboxylic acid. b) Reaction was carried out in DMF. c) as S-benzylthiuronium salt. d) Isolation was not carried out.

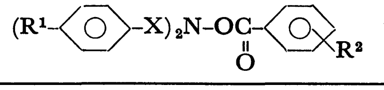
reaction of I ($R^1=H$; $R^2=p\text{-}NO_2$) with sodium p-chlorobenzenecarbothioate gave the addition product along with the expected products, indicating clearly that the imine (IV) is involved during these reactions.

On the other hand, there are two conceivable processes to give the imine (IV). The one is the base-catalyzed elimination of the carboxylate ion from the starting material (Path A) and the other, the decomposition of the initial product (II), which was formed by the nucleophilic substitution on the nitrogen atom, due to the instability of the N–Nu bond of II and then the nitrenium ion (III) will easily decompose to afford the imine (IV).[9)]

Isolation of the imine (IV) in the reaction of I ($R^1=Cl$; $p\text{-}R^2=NO_2$) with NaN_3 may be due to the increased stability of the imine (IV) intermediate, bearing electron-withdrawing p-chloro substituent.

Kinetics of the Reactions of I ($X=CH_2$; $Y=CO$; $R^1=CH_3$, H, Cl; $R^2=p\text{-}NO_2$, 3,5-$(NO_2)_2$) with NaN_3 and LiCl in DMSO. In order to make a choice between the two mechanisms (Path A and B) and to know the nature of these reactions in detail, we carried out the kinetic experiments using some substituted hydroxylamines (I) under pseudo-first order conditions with a large excess of nucleophiles. The over-all reaction rate was measured spectrophotometrically by following the increase in absorbance of p-nitro- and 3,5-dinitrobenzoate ions at 290 nm. Hydrogen–deuterium kinetic

TABLE 2. RATE CONSTANTS AND ACTIVATION PARAMETERS FOR THE REACTIONS OF THE HYDROXYL AMINES,



WITH NUCLEOPHILES IN DMSO

$(R^1\text{-}C_6H_4\text{-}X)_2N\text{-}OC(=O)\text{-}C_6H_4\text{-}R^2$

Nu[a)	R^1	X	R^2	Temp (°C)	10^5k (s^{-1})[b)	$\Delta H^{\neq}$ (kcal/mol)	$\Delta S^{\neq}$ (e.u.)	k_H/k_D
NaN_3	CH_3	CH_2	p-NO_2	30.0±0.1	6.46 ±0.50			
NaN_3	H	CH_2	p-NO_2	30.0	6.47 ±0.30	17.4	−20.2	
NaN_3	H	CD_2	p-NO_2	30.0	0.85 ±0.05			7.6
NaN_3	H	CH_2	p-NO_2	36.1	12.1 ±0.7			
NaN_3	H	CH_2	p-NO_2	42.0	20.2 ±0.9			
NaN_3	Cl	CH_2	p-NO_2	30.0	21.6 ±1.1			
NaN_3	H	CH_2	3,5-$(NO_2)_2$	30.0	75.0 ±2.0			
LiCl	H	CH_2	p-NO_2	30.0	1.41 ±0.12			
LiCl	H	CD_2	p-NO_2	30.0	0.173±0.018			8.1

a) Concentration of nucleophiles is 12 times excess, *i.e.*, [Substrates]$=6.9\times10^{-3}$ mol/l, [Nucleophiles] $=8.3\times10^{-2}$ mol/l. b) Pseudo-first order rate constants and error limits are standard deviation.

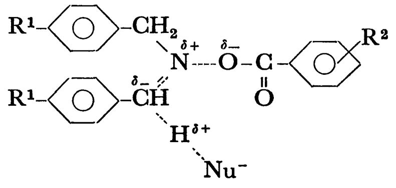
isotope effect was measured using the substrate which was labeled with D at the benzylic position of I under the same condition.

Good pseudo-first order kinetic behaviors were observed and the kinetic results are summarized in Table 2. As seen from Table 2, the isotope effects are 7.6 and 8.1 for the reactions of I (R^1=H; R^2=p-NO_2) with NaN_3 and LiCl as nucleophiles at 30 °C, respectively.

On the other hand, it has been generally known that secondary hydrogen isotope effects are $k_H/k_D=1.00$ for S_N2 reaction and $k_H/k_D=1.15$ for S_N1 reaction.[10) The isotope effect, thus, clearly indicates that the reaction is of base-catalyzed elimination (Path A). The order of the reactivities of the halide ions, $Cl^- > Br^- > I^-$, deduced from the recovered amounts of the starting material and the reaction times, also support that the reaction involves the rate-determining proton abstraction by the base.

The substituent effect (R^1) gave hardly any correlation with Hammett σ value. Apparently, an electron-withdrawing substituent such as Cl accelerated the reaction, while an electron-donating substituent (CH_3) could not retard it. On the other hand, the substituent effect (R^2) indicates the reaction rate to increase with the increase in electron-withdrawing ability of the substituent. This is also supported by the observation that the staring material was recovered in 63% yield for the reaction of I (R^1=H; R^2=p-OCH_3) with NaN_3, while no starting material was recovered in the reaction of I (R^1=H; R^2=p-NO_2) under the same condition. The activation parameters for the reaction of I (R^1=H; R^2=p-NO_2) with NaN_3 in DMSO are $\Delta H^{\neq}$, 17.4 kcal/mol and $\Delta S^{\neq}$, −20.2 *e.u.* respectively.

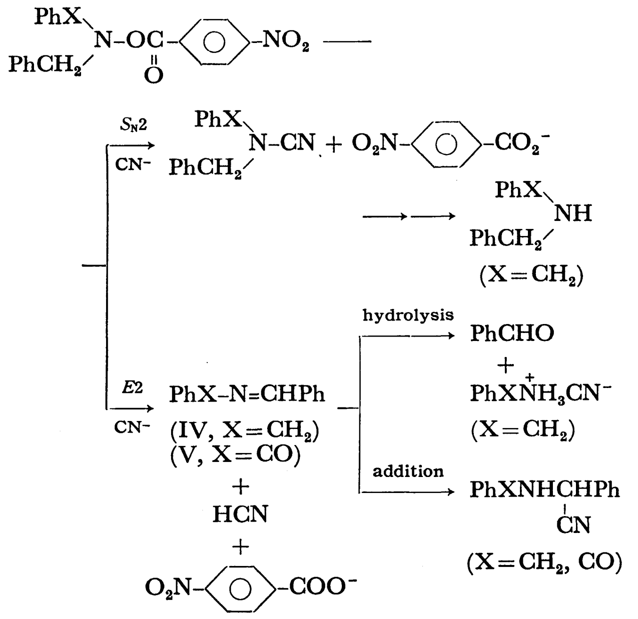
On the basis of these experimental observations, one can assume that the elimination reaction on the trivalent nitrogen atom involves the ionic transition state of an ideal concerted type like in the carbonyl-forming



elimination reaction of benzyl and 9-fluorenyl nitrates where primary hydrogen isotope effects are 5.94 for the former nitrate and 4.3 for the latter nitrate at 30 °C.[4b)

Reactions of I (X=CH_2, CO; Y=CO, SO_2; R^1=H; R^2=p-NO_2, p-Cl, p-OCH_3, 2,4,6-$(CH_3)_3$) with NaCN and KCN. The reaction of (I) (X=CH_2; Y=CO; R^2=p-NO_2) with NaCN in DMSO unexpectedly gave the dibenzylamine which may be formed *via N,N*-dibenzylcyanamide as the precursor in a substantial yield along with the products which were produced by the elimination (Path A). Among these products, the α-aminonitrile must be formed by the addition of HCN to the imine (IV). Although in a previous experiment[1) we have reported that the above reaction yields the *N,N*-dibenzylcyanamide, a careful reexamination revealed the cyanamide to be a mixture of dibenzylamine and an unidentified product bearing cyano group, which could not be separated from the other.

Meanwhile, a mechanism involving the nucleophilic attack of cyanide ion upon oxygen atom of the N–O bond in (I) seems to be unlikely since the anion of dibenzylamine is a very poor leaving group in DMSO.



Therefore, the scheme of the reaction with cyanide ion is depicted as follows.

Neither α-aminonitrile nor dibenzylamine was found among the products when the leaving group changes from *p*-nitrobenzoyloxy to 3,5-dinitrobenzoyloxy groups as seen in Table 1. In this reaction, a Meisenheimer-type complex would be formed in the main route like in the reaction of *O*-(3,5-dinitrobenzoyl)-*N*-aroyl-*N*-arylhydroxylamines with cyanide ion in DMSO[11] since a strong absorption band appeared at 602 nm immediately upon addition of NaCN. Furthermore, the final products were those which are expected by a minor path, *i.e.*, Path A.

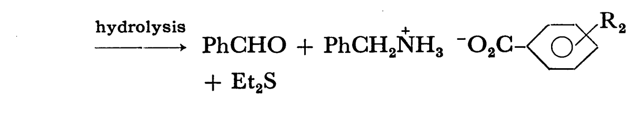
Here, it is interesting to examine the effect of substituents X, Y and R^2 on the product distribution, namely, the Substitution/Elimination ratio, since only the reaction with cyanide ion affords both substitution and elimination products on the nitrogen atom. The elimination-addition product, *i.e.*, α-benzoylamino-α-phenylacetonitrile, was obtained in a good yield by replacing a methylene group by a carbonyl group for the substituent X when substituents Y and R^2 are carbonyl and *p*-nitro groups. The yield of α-aminonitrile is better in DMSO than in DMF.

A similar tendency was observed in the reaction with I ($X=CO$; $Y=SO_2$; $R^2=2,4,6\text{-}(CH_3)_3$). Further inspection of the results in Table 1 reveals that introduction of more electron-donating substituents such as Cl and OCH_3 for R^2 in place of NO_2 group resulted in a predominant elimination according to Path A. Thus, the substitution product was shown to be obtained only when the substituents X, Y and R^2 are methylene, carbonyl and *p*-nitro groups, respectively. No formation of benzaldehyde in the reaction of I ($X=CO$; $Y=CO$; $R^2=p\text{-}NO_2$) with NaCN may be ascribed to the difference in stabilities of either the imine (IV) and (V) or the addition products which are obtained by the addition of HCN to the imine (IV) and (V). Accordingly, in the reaction with cyanide ion, the product distribution seems to be sensitive to the substituents R^2, X and Y.

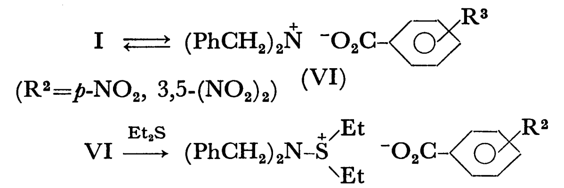
Reactions of I ($X=CH_2$; $Y=CO$; $R^1=H$; $R^2=$p-NO_2, 3,5-$(NO_2)_2$) with Diethyl Sulfide and p-*Toluenethiol.*

The reaction of I with nucleophiles such as sulfide and thiol is expected to proceed *via* nucleophilic substitution on the nitrogen atom at the initial step due to the very low proton affinity of these nucleophiles because the occurrence of elimination requires a high proton affinity of nucleophiles.

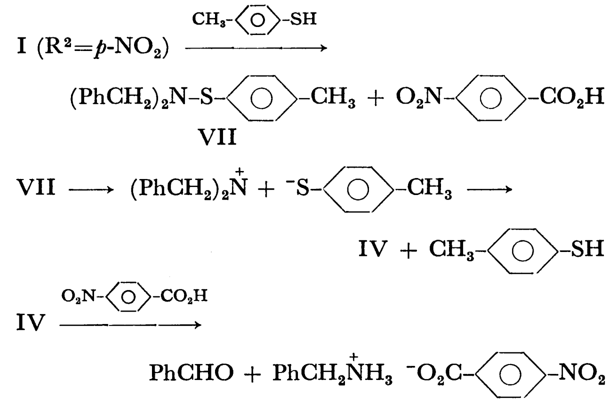
As indicated in Table 1, the reactions of I ($R^2=p\text{-}NO_2$, $3,5\text{-}(NO_2)_2$) with an excess of diethyl sulfide were found to give the products which are same as those in the reaction with NaN_3. Therefore, the following mechanism involving the initial nucleophilic substitution and the subsequent elimination appears to be the most plausible, judging from the nature of the nucleophile used.

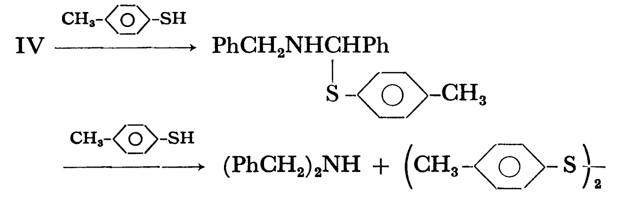


These results suggest the initial step of the reaction to proceed *via* a S_N2 path on the nitrogen atom like in the reaction of *O*-2,4-dinitrophenylhydroxylamine with phenyl methyl sulfide.[7a] One can also assume that these reactions proceed through the S_N1 path, namely, by forming dibenzylnitrenium ion as an intermediate because of the bulky benzyl groups, as shown below. If the ion-pair intermediate (VI) would exist, this very reactive nitrenium ion must yield benzaldehyde and benzylamine *via* the imine (IV). The starting material, however, was recovered nearly quantitatively when it was allowed to stand for 50 hr at room temperature in the absence of any nucleophile. Therefore, the S_N1 path seems to be unlikely, though no detailed mechanism for this reaction can be elucidated at present.



In the reaction with *p*-toluenethiol, a same reaction scheme as above may be applied on the basis of product distribution in Table 1. The sulfenamide (VII) which was produced by a S_N2 reaction on the trivalent nitrogen atom at the initial step will decompose to give the nitrenium ion and *p*-toluenethiolate ion. No formation of dibenzylamine excludes the following two possibilities, namely, the nucleophilic attack of the thiol upon the sulfur atom of the sulfenamide (VII) giving dibenzylamine and the disulfide, and the addition of the thiol to the imine affording dibenzylamine and the disulfide as shown below. The





disulfide obtained may be formed by the oxidation of the thiol in DMF. This is confirmed by the control experiment independently.

Recently, Krueger *et al.*[7b)] have shown that for substitution on the trivalent nitrogen atom polarizability of the nucleophile plays a major role, with basicity making a minor contribution. Their results support the earlier prediction by Edwards and Pearson.[12)]

In the reactions of (I) ($X=CH_2$; $Y=CO$; $R^1=H$; $R^2=p\text{-}NO_2$) with various nucleophiles in DMSO, proton affinity (basicity) of the nucleophiles plays an important role, since the elimination can compete with the nucleophilic substitution on the nitrogen atom in this model compound (I). Thus, reactions with charged nucleophiles such as N_3^-, X^- ($X=Cl$, Br, I) and OH^- underwent elimination reaction, while reactions with sulfide and thiol underwent nucleophilic substitution at the initial step despite the presence of a bulky benzyl group.

Experimental

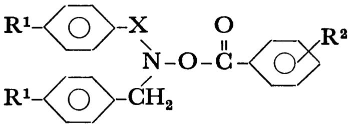
Materials. *N,N*-Dibenzylhydroxylamine was prepared according to the method of L. W. Jones and C. N. Sneed, mp 123—124 °C (lit, 124 °C).[13)] *N*-Benzoyl-*N*-benzylhydroxylamine was prepared by the reaction between benzoyl chloride (1 mol) and *N*-benzylhydroxylamine (2 mol), which was synthesized according to the method of L. W. Jones and C. N. Sneed, in dry ether at 0 °C. Recrystallization from ethanol-water gave white needles, mp 107—108 °C. *O*-Aroyl-*N,N*-di(*p*-substituted benzyl)- and *O*-aroyl-*N*-benzoyl-*N*-benzylhydroxylamines were obtained by the reactions of aroyl chlorides with *N,N*-di(*p*-substituted benzyl)hydroxylamines, and with *N*-benzoyl-*N*-benzylhydroxylamine respectively under usual Schotten-Baumann conditions. The physical properties of these hydroxylamines are listed in Table 3.

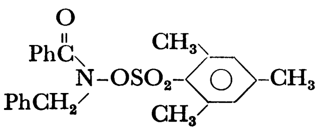
Solvents. Dichloromethane was distilled after drying over calcium chloride and acetonitrile was distilled over phosphorus pentoxide. Dimethyl sulfoxide was distilled twice over activated alumina and *N,N*-dimethylformamide was distilled under reduced pressure.

Nucleophiles. Alkali-metal azide, halides, hydroxide and cyanide were all commercial products which were used without further purification other than drying at 100—120 °C overnight *in vacuo*. Sodium *p*-chlorobenzenecarbothioate was prepared from the reaction of *p*-chlorothiobenzoic acid with sodium hydroxide and was used without further purification after drying *in vacuo*. Diethyl sulfide and *p*-toluenethiol were used after purification by distillation.

General Procedure for the Reactions of O-Aroyl-N,N-di(p-substituted benzyl)hydroxylamines with Nucleophiles such as NaN_3, *LiCl, NaI, NaOH, and* $NaSCOC_6H_4Cl$-*p*. A small excess of a nucleophile (2.3—3.0 mmol) was added into DMSO (8 ml) solution of the hydroxylamine (2.0—2.3 mmol) in a reaction vessel and the whole solution was stirred with magnetic stirrer at room temperature for 15—50 h. After the reaction had subsided, the reaction mixture was poured into water (120 ml) and then products were extracted twice with dichloromethane (40 ml). The dichloromethane solution was washed with water several times and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded the residual oil, which was then chromatographed on silica gel, eluting with dichloromethane. The aqueous layer was acidified slightly with dil-HCl aqueous solution and extracted twice with chloroform (60 ml), which was then washed with water several times. After drying over anhydrous sodium sulfate, evaporation of chloroform gave the crude *p*-nitro- and 3,5-dinitrobenzoic acids. Next, the acidic aqueous solution was made alkaline with sodium carbonate and extracted twice with dichloromethane (40 ml), and dried over anhydrous sodium sulfate. Removal of solvent *in vacuo* gave *p*-substituted benzylamines.

TABLE 3. PHYSICAL PROPERTIES OF HYDROXYLAMINES,



R^1	X	R^2	mp (°C)	Anal. %, Found (Calcd)			IR (KBr) ν_{CO},cm^{-1}	NMR ($CDCl_3$), δ
				C	H	N		
H	CO	*p*-NO_2	112.5—114.5	66.82 (67.01)	4.30 (4.29)	7.48 (7.44)	1780, 1670	5.03 (s, 2H), 7.12—7.72 (m, 10H), 8.01 (dd, 4H)
H	CH_2	*p*-OCH_3	83—84	75.90 (76.06)	6.05 (6.09)	3.90 (4.03)	1725	3.73 (s, 3H), 4.18 (s, 4H), 6.81 (dd, 4H), 7.10—7.60 (m, 10H)
H	CH_2	*p*-Cl	82—83	71.43 (71.69)	5.19 (5.16)	3.80 (3.98)	1740	4.20 (s, 4H), 7.15—7.95 (m, 14H)
H	CH_2	*p*-NO_2	108—109	69.71 (69.60)	5.08 (5.01)	7.64 (7.73)	1750	4.20 (s, 4H), 7.03—7.55 (m, 10H), 7.84 (dd, 4H)
H	CH_2	3,5-$(NO_2)_2$	148—149	62.03 (61.91)	4.30 (4.21)	10.19 (10.31)	1755	4.32 s(, 4H), 7.13—7.61 (m, 10H), 8.79—8.90 (m, 2H), 9.03—9.17 (m, 1H)
CH_3	CH_2	*p*-NO_2	111—113	70.78 (70.75)	5.83 (5.68)	6.98 (7.17)	1740	2.24 (s, 6H), 4.13 (s, 4H), 7.45 (dd, 8H), 7.91 (dd, 4H)
Cl	CH_2	*p*-NO_2	133—134	58.46 (58.48)	3.82 (3.74)	6.44 (6.49)	1740	4.20 (s, 4H), 7.08—7.50 (m, 8H), 7.99 (dd, 4H)
			129—130	67.83 (67.46)	5.69 (5.66)	3.23 (3.42)	1670	2.26 (s, 3H), 2.55 (s, 6H), 5.06 (s, 2H), 6.83 (s, 2H), 7.02—7.45 (m, 10H)

Structures of the products isolated were identified by comparing their physical properties with those of the authentic compounds.

N-*Benzylidenebenzylamine,* which was obtained in the reaction with NaOH, was hydrolyzed to give benzaldehyde and benzylamine when the imine obtained was passed through silica gel column. Therefore, yields of the imine and benzaldehyde were determined before separation by means of NMR spectroscopy.

Addition product, i.e., α-benzylaminobenzyl p-*chlorobenzenecarbothioate,* which was isolated in the reaction with sodium *p*-chlorobenzenecarbothioate, was recrystallized from benzene–hexane to give colorless needles, mp 162—163 °C; IR (KBr) 3300, 1640 cm^{-1}; NMR ($CDCl_3$) δ 4.51 (s, 1H), 4.61 (s, 2H), 6.86 (broad s, 1H), 7.13—7.90 (m, 14H); Anal. Found: C, 68.60; H, 4.77%. Calcd for $C_{21}H_{18}NOSCl$: C, 68.56; H, 4.93%.

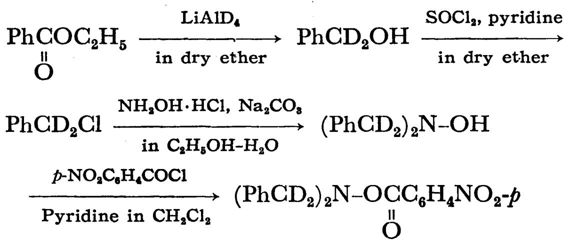
Reactions of O-*(*p-*Substituted Benzoyl)*-N,N-*dibenzylhydroxylamines with Cyanide Ion.* A typical run was as follows: to the *O*-(*p*-nitrobenzoyl)-*N,N*-dibenzylhydroxylamine (2.6 mmol) in DMSO (7 ml) was added NaCN (2.7 mmol) at room temperature. After 15 h, the reaction mixture was poured into water (120 ml) and then products were extracted twice with dichloromethane (40 ml). After drying over anhydrous sodium sulfate, solvent was evaporated *in vacuo.* The resulting residue was subjected to column chromatography packed with silica gel using dichloromethane as eluent, and three fractions, benzaldehyde (7%), α-benzylamino-α-phenylacetonitrile (22%) and dibenzylamine (58%) were obtained respectively. *p*-Nitrobenzoic acid (87%) and benzylamine (8%) were isolated by similar work-up as above. Structures of the products were determined in comparison with authentic samples. The α-aminonitrile was colorless oily liquid; IR (neat) 3330, 2225 cm^{-1}; NMR ($CDCl_3$) δ 1.80 (s, 1H), 3.83 (s, 2H), 4.58 (s, 1H), 7.09—7.63 (m, 10H). This α-aminonitrile was allowed to react with an equimolar amount of *p*-nitrobenzoyl chloride to afford α-*p*-nitrobenzoylbenzyl-α-phenylacetonitrile in 87% yield, which was recrystallized from benzene to give pale yellow needles, mp 148—149 °C; IR (KBr) 1645, 1525, 1350 cm^{-1}, ν_{CN} was too weak to detect; NMR ($CDCl_3$) δ 4.52 (dd, 2H), 6.73 (s, 1H), 6.86—7.42 (m, 5H), 7.47 (s, 5H), 7.92 (dd, 4H); Anal. Found: C, 71.76; H, 4.56; N, 11.24%. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31%.

Reactions of O-*Aroyl*-N-*benzylhydroxylamines with Cyanide Ion.* For a typical run, a mixture of *O*-(*p*-nitrobenzoyl-*N*-benzoyl-*N*-benzylhydroxylamine (2.2 mmol) and NaCN (2.7 mmol) was dissolved in DMSO (8 ml) in a reaction vessel, and the mixture was stirred for 15 h at room temperature. The contents were then poured into water (120 ml), the solution was extracted, and the products were separated by column chromatography through silica gel using dichloromethane as eluent. The product obtained was α-benzoylamino-α-phenylacetonitrile (58%) which was recrystallized from benzene–hexane, mp 147.5—148.5 °C; IR (KBr) 3250, 2220, 1640 cm^{-1}; NMR ($CDCl_3$) δ 6.32 (d, 1H), 7.24—8.04 (m, 11H); Mass spectrum *m/e* 236 (parent); Anal. Found: C, 76.46; H, 5.06; N, 11.84%. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86%. Acid-catalyzed methanolysis of this product in refluxing methanol–HCl gave methyl α-benzoylamino-α-phenylacetate (90%) which had mp 113.5—114.5 °C; IR (KBr) 3280, 1760, 1635 cm^{-1}; NMR ($CDCl_3$) δ 3.76 (s, 3H), 5.80 (d, 1H), 7.05—7.98 (m, 11H). The aqueous layer was acidified with dil-HCl aqueous solution and extracted twice with chloroform (60 ml). The chloroform solution was dried over anhydrous sodium sulfate after washing with water several times, followed by evaporation of chloroform afforded crude *p*-nitrobenzoic acid in 27% yield, identical with the authentic sample.

Reactions of O-*(*p-*Nitrobenzoyl)- and* O-*(3,5-Dinitrobenzoyl)*-N,N-*dibenzylhydroxylamines with Diethyl Sulfide and* p-*Toluenethiol.* A typical run was as follows: to *O*-(*p*-nitrobenzoyl)-*N,N*-dibenzylhydroxylamine (2.2 mmol) in DMSO (7 ml) was added diethyl sulfide (3.0 mmol) at room temperature and the whole solution was allowed to stand for 48 h. A similar work-up as in the above experiment gave recovered starting material (28%), benzaldehyde (49%), *p*-nitrobenzoic acid (38%) and benzylamine (33%).

In the reaction with *p*-toluenethiol, two molar amount of *p*-toluenethiol was allowed to react with the hydroxylamine in DMF at room temperature. Separation and identification of the products obtained were carried out similarly.

O-(p-*Nitrobenzoyl*)-N,N-*di(benzyl*-α-d$_2$*)hydroxylamine* was prepared according to the following reaction steps.



$$\underset{\overset{\|}{O}}{PhCOC_2H_5} \xrightarrow[\text{in dry ether}]{LiAlD_4} PhCD_2OH \xrightarrow[\text{in dry ether}]{SOCl_2,\ \text{pyridine}}$$

$$PhCD_2Cl \xrightarrow[\text{in } C_2H_5OH\text{-}H_2O]{NH_2OH\cdot HCl,\ Na_2CO_3} (PhCD_2)_2N\text{-}OH$$

$$\xrightarrow[\text{Pyridine in } CH_2Cl_2]{p\text{-}NO_2C_6H_4COCl} (PhCD_2)_2N\text{-}O\underset{\overset{\|}{O}}{C}C_6H_4NO_2\text{-}p$$

O-(*p*-Nitrobenzoyl)-*N,N*-di(benzyl-α-*d*$_2$)hydroxylamine obtained was recrystallized twice from benzene–hexane to give pale yellow needles, 700 mg (total yield, 11%) which had mp 108—109 °C. The NMR showed no proton of the methylene groups.

Procedure for Kinetic Runs. Each kinetic run was carried out by monitoring the UV absorbance of *p*-nitro- and 3,5-dinitrobenzoate ions liberated during the reaction at 290 nm. At first the solution of *O*-aroyl-*N,N*-di(*p*-substituted benzyl) hydroxylamines in 10 ml of DMSO (13.8×10^{-3} mol/l) was placed in a reaction vessel and immersed in a constant temperature bath which was kept at 30.0±0.1 °C. The solution of a nucleophile such as NaN_3 or LiCl in 10 ml of DMSO (16.6×10^{-2} mol/l), which was previously kept at 30.0±0.1 °C in a same constant temperature bath, was added to the DMSO solution of the hydroxylamine. The reaction was followed by taking out 0.5 ml aliquot at suitable time intervals, diluting the aliquot with 50 ml of acetonitrile–water (2:1 in volume), and finally subjecting the solution for measurement of the optical density of the resulting solution at 290 nm. All the pseudo-first order rate constants were determined from following rate equation and the extent of reaction studied was *ca.* half-life.

$$\log(a_\infty - a_0) - \log(a_\infty - a_t) = (k/2.303)t$$

a_∞; the final absorbance at 290 nm,
a_0; the initial absorbance at 290 nm,
a_t; the absorbance at 290 nm after t.

For a typical run, molar extinction coefficients of *O*-(*p*-nitrobenzoyl)-*N,N*-dibenzylhydroxylamine, sodium *p*-nitrobenzoate, benzaldehyde, *N*-benzylidenebenzylamine and benzylamine in acetonitrile-water (2:1 in volume) were 4400, 7200, 1000, 400 and 0 at 290 nm respectively. Effect of the absorbance of benzaldehyde seems to be negligibly small since a good pseudo-first order kinetic behavior was observed in each case.

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