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Oxidation of Dibenzylhydroxylamines to Nitrones. Effects of Structure and Oxidizing Agent on Composition of the Products

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A group of dibenzylhydroxylamines bearing a para substituent (nitro, chloro, methyl, methoxy), a meta substituent (nitro, methoxy), or an ortho substituent (nitro, chloro, methoxy) as well as the *p*-methoxy-*p'*-nitro derivative, and the α-phenyl derivative, was treated with the oxidizing agents *N*-bromosuccinimide, (diacetoxyiodo)benzene, mercuric oxide, iodine, *tert*-butyl hydroperoxide, or ceric ammonium nitrate. The products were pairs of isomeric substituted *N*-benzyl-α-phenylnitrones; the compositions were determined by NMR. The isomer ratios differed from the known equilibrium ratios, in most cases only moderately, but markedly with the *p*-methoxy-*p'*-nitro and the α-phenyl examples; these facts imply kinetic control of product composition. Isomer ratios generally varied with the oxidizing agent used from slightly to moderately, a circumstance not altogether consistent with a common product-determining step, such as disproportionation of an intermediate nitroxide. Oxidations with mercuric oxide differed noticeably from those with the other oxidizing agents, especially in the cases with ortho substituents. Variation among oxidizing agents was marked with the α-phenyl derivative. Alternative product-determining steps, not involving nitroxide disproportionation, appear to be involved.

Oxidation of N,N-disubstituted hydroxylamines to nitrones (eq 1) has long been known, and occurs easily with a variety of oxidizing agents and in good yields. Although no

$$(R_2CH)_2NOH \xrightarrow{(O)} R_2C{=}N(O){-}CHR_2 \qquad (1)$$

general study of this reaction has been reported,[2] it has generally been presumed to proceed by a one-electron oxidation to an intermediate nitroxide radical. Support for this view is to be found in the work of Sheina and Gallai,[3] who observed a one-electron stage in the electrolytic oxidation of *N*-phenyl-*N*-benzylhydroxylamine, and that of Gutch and Waters,[4] who observed ESR signals corresponding to nitroxides during oxidation of several hydroxylamine derivatives with ceric ion or ferricyanide.

Oxidation of dibenzylhydroxylamine by oxygen in basic solution has been studied kinetically by Cowley and Waters,[5] who followed the appearance of the ESR signal of dibenzyl nitroxide. The second stage in the reaction was presumed to be disproportionation of the nitroxide into benzaldehyde *N*-phenylnitrone and dibenzylhydroxylamine (eq 2), but it was not specifically investigated.

$$(PhCH_2)_2NOH \xrightarrow[OH^-]{O_2} (PhCH_2)_2NO\cdot$$

$$2(PhCH_2)_2NO\cdot \longrightarrow PhCH{=}N(O){-}CH_2Ph + (PhCH_2)_2NOH \qquad (2)$$

Oxidation of hydroxylamines bearing two different N substituents appears not to have been studied, except for the work of Johnson, Rodgers, and Trappe[6] on the autoxidation of *N*-methyl-*N*-ethyl- and *N*-methyl-*N*-propylhydroxylamine, and certain cases where only one of the substituents bore an α hydrogen, and was thus oxidizable. If both substituents have α hydrogens, one would expect a pair of isomeric nitrones to be formed. If the ratio of isomers is thermodynamically determined, it would be identical with that determined from experiments on the equilibration of nitrones, modified slightly by any necessary differences in experimental conditions (i.e., temperature and solvent), but if the ratios are kinetically controlled, some differences from the equilibrium ratios might be found. If disproportionation of an intermediate nitroxide is the product-forming stage in the oxidation, the isomer ratios obtained would be the same, regardless of the oxidizing agent, even if kinetically determined. However, if the oxidizing agent is involved in the product-forming step, the isomer ratios might be sensitive to the nature of the oxidizing agent, presuming kinetic control.

We have undertaken a study of the ratios of isomeric nitrones produced from substituted dibenzylhydroxylamines, using a variety of oxidizing agents. We anticipated that the results would clarify some of the features of the mechanism, and would also have some practical value for the prediction of the major product to be expected where two are possible.

Results

A series of *N,N*-dibenzylhydroxylamines was prepared by treatment of monobenzylhydroxylamines[7] with benzyl halides in the presence of sodium carbonate. The yields and properties are reported in Table I. α-Phenyldibenzylhydroxylamine (*N*-benzyl-*N*-benzhydrylhydroxylamine) was prepared by the reaction of phenylmagnesium bromide with benzaldehyde-*N*-phenylnitrone.

Oxidations were carried out with *N*-bromosuccinimide in chloroform in the presence of pyridine or other amine, with (diacetoxyiodo)benzene (phenyliodoso acetate) in methylene chloride in the presence of cyclohexylamine, with

Table I
Dibenzylhydroxylamines[a] $YC_6H_4CH_2N(OH)CH_2C_6H_4Z$ from $YC_6H_4CH_2NHOH$ and $ZC_6H_4CH_2X$

Registry no.	Substituent Y	Source Z	Source X	Yield, %[b]	Mp, °C	NMR, δ
55648-93-6	*p*-NO_2	H	Br	79	127–128[c]	3.79 (s, 4 H)
55648-94-7	*p*-Cl	H	Cl	56	105–106	2.60 (s, 2 H), 2.66 (s, 2 H)
55648-95-8	*p*-CH_3	H	Cl	54	96–99	2.26 (s, 3 H), 3.64 (s, 4 H)
55648-96-9	*p*-CH_3O	H	Br	27	95–96.5	3.66 (s, 3 H), 3.68 (s, 4 H)
55648-97-0	*m*-NO_2	H	Br	30	97.5–100	3.78, 3.80 (singlets, 4 H total)
55648-98-1	*m*-CH_3O	H	Br	47	58–59	3.64, 3.66, 3.72 (singlets, 7 H total)
55648-99-2	*o*-NO_2	H	Br	49	93–95	3.79 (s, 2 H), 4.12 (s, 2 H)
55649-00-8	*o*-Cl	*o*-Cl	Cl	75	91–92.5	3.64 (s, 2 H), 3.76 (s, 2 H)
55649-01-9	*o*-CH_3O	H	Br	39	121–123	3.54, 3.64, 3.68 (singlets, 7 H total)
55649-02-0	*o*-CH_3O	*p*-NO_2	Br	29.5	118–119	3.84 (s, 4 H), 3.76 (s, 3 H)

[a] Satisfactory analyses for C, H, and N (±0.25%) were obtained for all new compounds. [b] After one or more recrystallizations; yields of crude product were in most cases nearly twice as great. [c] Lit.[30] mp 125.5–126.5°.

Table II
Ratios of Isomeric Nitrones Obtained by Oxidation of Dibenzylhydroxylamines $YC_6H_4CH_2N(OH)CH_2C_6H_4Z$

A = $YC_6H_4CH_2N(\rightarrow O)=CHC_6H_4Z$; B = $YC_6H_4CH=N(\rightarrow O)CH_2C_6H_4Z$

Hydroxylamine, substituents		Oxidizing agent[a] NBS		$PhI(OAc)_2$		HgO		I_2		*t*-BuOOH		$Ce(NH_4)_2(NO_3)_6$		Registry no.	
Y	Z	% B	A/B	% B	A/B	% B	A/B	% B	A/B	% B	A/B	% B	A/B	A	B
p-NO_2	H	58.5	0.71	66.5	0.50	68.5	0.46	62.0	0.61	62.5	0.60	*g*		22661-28-5	22661-23-0
p-Cl	H	54.5	0.83	59.0	0.69	62.0	0.61	61.5	0.63	58.5	0.71	57.0	0.75	55606-33-2	22687-09-8
p-CH_3	H	48.0[b]	1.09	49.5[b]	1.02	56.5[b]	0.77							55606-34-3	55606-41-2
p-CH_3O	H	51.5	0.94	50.5	0.98	52.5	0.90	55.5	0.80	54.5	0.83			55606-35-4	32114-41-3
m-NO_2	H	56.0	0.79	61.1	0.64	66.5	0.50	59.5	0.68					55606-38-7	5367-21-5
m-CH_3O	H	48.0	1.09			49.5	1.02	55.5	0.80					55606-39-8	55606-43-4
o-NO_2	H	56.6	0.77	51.5	0.94	45.0	1.22							22661-27-4	22661-22-9
o-Cl	H	55.0	0.82	49.0	1.04	44.0	1.27							55606-36-5	22687-07-6
o-CH_3O	H	28.0	2.56	37.5	1.67	33.5	2.00							55606-37-6	55606-42-3
p-CH_3O	*p'*-NO_2	34.0	1.92	32.5	2.08	27.0	2.70	26.5	2.78					55606-40-1	55606-44-5
Ph_2CHNCH_2Ph[h] | OH		89.0[c]	0.12	71.0	0.41	50.5	0.98	72.0	0.39			*i*		3376-29-2	3376-27-0
		82.5[d]	0.21												
		84.5[e]	0.18												
		86.0[f]	0.16												

[a] The figures in the columns are averages of duplicate determinations made on the results of duplicate experiments. [b] One determination only. [c] In presence of pyridine. [d] In presence of cyclohexylamine. [e] In presence of 2,6-lutidine. [f] In presence of triethylamine. [g] Extensive hydrolysis vitiated the results. [h] A = α,α-diphenyl-*N*-benzylnitrone; B = α-phenyl-*N*-benzhydrylnitrone. [i] Did not react.

mercuric oxide suspended in ether, with iodine in chloroform in the presence of pyridine, with *tert*-butyl hydroperoxide in benzene, and with ceric ammonium nitrate in water overlaid with ether. The progress of the reactions was followed by TLC, and when no more hydroxylamine remained, the unwanted substances were removed and the mixtures of nitrones were analyzed by NMR in the manner previously described. In general, duplicate experiments were carried out for each situation, and duplicate determinations were made for each experiment. The results are reported in Table II in two forms: the percent of the isomer derived from the substituted benzaldehyde, and the ratio of the two isomers. The total yields of nitrones, determined by weighing the isolated products before analysis, were in all cases between 90 and 99%.

With three of the oxidizing agents that required base [NBS, $PhI(OAc)_2$, I_2], the effect of changing from pyridine to cyclohexylamine, involving a difference of five powers of ten in base strength, was examined in the oxidation of *N*-benzyl-*N*-benzhydrylhydroxylamine. There was no significant difference in product ratio with the latter two oxidizing agents, but with NBS, an increase in the proportion of isomer B from 82.5 to 89% was observed, reproducible in three independent experiments. However, 2,6-lutidine did not show this effect, and 1,4-diazabicyclo[2.2.2]octane (triethylenediamine) showed a difference of only 3.5%, close to the limit of reliability of the determinations.

The effect of degree of completion of oxidation on the product ratio was investigated with mercuric oxide oxidation of *p*-nitro- and *p*-chlorodibenzylhydroxylamine and with oxidation of *p*-methoxydibenzylhydroxylamine oxidizing by *tert*-butyl hydroperoxide. The values were constant from 13 to 100% of completion, within the reliability of the determinations. A wider selection of experiments was not feasible for technical reasons. Table III shows the results with mercuric oxide.

The possibility that nitrone, once formed, might be slowly isomerized toward the equilibrium ratio was examined extensively, by conducting oxidations of hydroxylamines to which a known amount of one of the nitrones had been added. With NBS (eight different hydroxylamines), (diacetoxyiodo)benzene (seven hydroxylamines), mercuric oxide (seven hydroxylamines), and iodine (four hydroxylamines), the ratios of isomeric nitrones observed at completion were identical, within the estimated experimental error, with the ratios calculated from those of simple oxidations and the

Table III
Effect of Degree of Completion of Oxidation on Product Ratios

Extent of reaction, %	% of B in nitrones produced: Y = *p*-NO_2	Y = *p*-Cl
13		64.2
46.5		60.1
67.5	68.2	
100	68.5	62.0

Table IV
Effect of Added Nitrone on Product Ratios in Oxidation of Dibenzylhydroxylamines by Iodine

$YC_7H_6N(OH)CH_2C_6H_5 \longrightarrow$
$YC_7H_6N(\rightarrow O)=CHC_6H_5$ (A) and $YC_7H_5=N(\rightarrow O)CH_2C_6H_5$ (B)

Y	Hydroxylamine, g	Nitrone added, g	% of B in product: Calcd	Found
p-NO_2	0.2	B (0.1)	74.6	76.8, 77.6
p-Cl	0.2	B (0.1)	74.0	73.6, 74.1
p-CH_3O	0.2	B (0.1)	70.6	70.2, 69.2
α-C_6H_5	0.2	B (0.1)	48.1	49.0, 49.0

assumption that the added nitrone remained unaltered throughout. The results obtained in the case of iodine oxidations are representative, and are presented in Table IV. In other experiments, pure nitrones were treated with oxidizing agents under the same experimental conditions; the recovered nitrones had not been isomerized.

Discussion

The foregoing results are best considered in the context of what is known about the oxidation of tertiary amines in general, of which N,N-disubstituted hydroxylamines constitute a special case. Two types of mechanism have been proposed, differing according to the initial (presumably rate-determining) step: removal of an electron from nitrogen to form an aminium cation radical, $R_3N\cdot^+$, or abstraction of hydride from an α carbon to form an aminocarbonium ion (immonium ion), $R_2N^+{=}CHR'$. In the former, the initial step is not product determining, but in the latter it is.

Abstraction of hydride has been considered principally in connection with oxidation by aqueous bromine[8] or triphenylmethyl carbonium ions.[8,9] For *N*-methyldibenzylamines with a substituent on one benzyl group, Hammett regression constants of −0.84 (aqueous Br_2) and −2.0 (Ph_3C^+) for oxidation to immonium ions were reported. This selectivity for different α hydrogens is consistent with the results of hydride extraction from other classes of substrate; electron-withdrawing substitution retards hydride abstraction, and electron donation facilitates it. This behavior is opposite to our experimental results with dibenzylhydroxylamines with nitro substituents. It can therefore be concluded that hydride abstraction is not the major pathway for oxidation of any of the oxidizing agents used in this study. (Hull et al.[10] have presented evidence that hydride abstraction may compete as a minor pathway with electron abstraction by ClO_2 as oxidizing agent for tertiary amines.)

Formation of an aminium cation radical as the first step in oxidation of tertiary amines has been demonstrated for a variety of oxidizing conditions, and the rates have been correlated with the ionization potentials of the amines. Ferricyanide ion,[11] cupric ion,[12] dibenzoyl peroxide,[11] chlorine dioxide,[13] and electrolytic oxidation[13,14] are among the means studied. Product distribution from such oxidations of unsymmetrical tertiary amines has been less extensively studied, but investigations with substituted benzyldimethylamines conform to the generalization that factors that increase the acidity of an α hydrogen favor oxidation of that site to an alkylidene moiety (eq 3).[11,15,16] It should

$$ArCH_2N(CH_3)_2 \xrightarrow{(O)} ArCH{=}N^+(CH_3)_2 \text{ and } ArCH_2\underset{\displaystyle CH_3}{\overset{|}{N^+}}{=}CH_2 \quad (3)$$

be noted that this is the opposite of the effect with hydride abstraction.

Audeh and Smith[11] have proposed that the product-determining step is loss of a proton from an α carbon of the aminium cation radical, a step that they expressed as an irreversible reaction, followed by oxidation of the resulting α-aminoalkyl radical to an immonium ion (eq 4). In the

$$(RCH_2)_3\overset{+}{N}\cdot \xrightarrow{-H^+} (RCH_2)_2N{-}\dot{C}HR \xrightarrow{(O)} (RCH_2)_2\overset{+}{N}{=}CHR \quad (4)$$

case of *N,N*-dialkylhydroxylamines, the hydroxyl group bears the most eminently acidic hydrogen, loss of which to form a nitroxide should predominate overwhelmingly over deprotonation from an α carbon. Such a step would not, however, be product determining; instead, the succeeding oxidation step to convert the nitroxide to a nitrone would fulfill that role.

If the assumption of Cowley and Waters[5] is correct that in the oxidation of hydroxylamines to nitrones, conversion of intermediate nitroxides to nitrones takes place by disproportionation, the product-determining step would be the same, regardless of the oxidizing agent used (cf. eq 2). Two other pathways deserve consideration. One of these assumes that deprotonation of hydroxylaminium cation radicals is actually reversible, and that the nitroxide or its conjugate acid may also be deprotonated at carbon, albeit very slowly (eq 5, 6). The product-determining step would

$$(RCH_2)_2N{-}O\cdot \underset{-H^+}{\overset{H^+}{\rightleftharpoons}} (RCH_2)_2\overset{+}{N}{-}OH \longrightarrow RCH_2N(OH)\dot{C}HR \quad (5)$$

$$RCH_2N(OH)\dot{C}HR \xrightarrow{(O)} RCH_2N(\rightarrow O){=}CHR \quad (6)$$

then be the same as that for oxidation of tertiary amines. The product distribution would be determined largely by the relative acidities of the α hydrogens and would also be independent of the oxidizing agent used so long as the last oxidation step is faster than reprotonation of the carbon radical to reform the hydroxylaminium cation radical. This mechanism was invoked by Johnson, Rodgers, and Trappe to explain their observation that autoxidation appeared to involve only the methyl group of *N*-methyl-*N*-alkyl hydroxylamines in basic medium.[6]

An alternative is that the nitroxide (or its conjugate acid) is attacked by more oxidizing agent, in effect removing H·, and thereby forming nitrone directly (eq 7). With such a

$$(RCH_2)_2N{-}O\cdot \xrightarrow{(O)} RCH_2N(\rightarrow O){=}CHR \quad (7)$$

mechanism, the product distribution would show some sensitivity to the oxidizing agent used. The results shown in Table II show that such a dependence, varying from slight to moderate, does exist. It may be presumed to involve both the electronic demand of the oxidizing agent and its steric requirements. Mercuric oxide deviates more than the other oxidizing agents, a circumstance that must be con-

nected with the fact it is the only one of the group in which oxidation takes place on a solid surface.

Observation of a dependence of product distribution on oxidizing agent limits the mechanisms of eq 2, 5, and 6 to a minor role in the oxidation of hydroxylamines in comparison with eq 7. However, it does not preclude a minor competitive role for the deprotonation pathway of eq 6. For situations in which the rates of the two pathways are not extremely different, their relative importance might be influenced by changes in basicity of the reaction medium in such a way as to be reflected in observable changes in product ratio. The observations of the effect of different bases on oxidation by NBS may perhaps be due to an effect of this sort.

Some incidental observations on the effect of degree of completion of oxidation on product ratios provide further evidence against a significant role for the disproportionation path (eq 2); the reaction is second order in nitroxide in eq 2 but first order in eq 7. If the concentration of nitroxide varies in proportion to concentration of the hydroxylamine from which it is produced, the disproportionation path would contribute less toward the end of the reaction, so long as a substantial excess of oxidizing agent is present. The product distribution would thus vary with the stage of completion of the oxidation if the two pathways independently resulted in different product ratios. No dependence on degree of completion was observed in a limited variety of experiments (Table III). This evidence does not rigorously exclude disproportionation as a contributing pathway, but it does mean that either its contribution must be small, or the product distributions from the two paths are not substantially different.

We had originally considered that eq 7 might in some instances be sufficiently reversible to provide a path for the isomerization of unsymmetrical nitrones, alternative to the base-catalyzed prototropy examined in the accompanying paper. However, the fact that our oxidations produced mixtures of kinetically determined composition demonstrates that the reduced forms of the oxidizing agents used do not promote isomerization significantly. In addition, we attempted to equilibrate α-(*o*-chlorophenyl)-*N*-benzylnitrone by treatment with ferrous sulfate in ethanol, but no isomerization could be detected after 18 hr. Equation 7 is evidently not significantly reversible under the conditions of our experiments; eq 6, however, could be reversible without effecting equilibration of isomers.

In summary, the whole evidence points to the fact that in the oxidation of hydroxylamines to nitrones, the distribution of isomeric nitrones is determined kinetically, primarily by a step in which an intermediate nitroxide reacts with a second equivalent of oxidizing agent; alternative pathways may compete under certain circumstances, but their contribution remains essentially secondary. It is possible to influence the product distribution by choice of oxidizing agent; the effect is generally small among substrates with only electronic differences at the site of oxidation, somewhat larger where steric differences are involved. Iodine and mercuric oxide are somewhat more selective than NBS or (diacetoxyiodo)benzene.

Experimental Section

NMR spectra were determined on a Varian A-60 instrument, or, where specified, an A-100 instrument, using $CDCl_3$ solutions with tetramethylsilane as internal reference. Melting points are uncorrected. Thin layer chromatograms were prepared with Eastman Chromagram Type 6060 sheets (silica gel with fluorescent indicator) using chloroform or ethanol–chloroform mixtures for development. Analyses are by Spang Microanalytical Laboratory, Ann Arbor, Mich.

Dibenzylhydroxylamines. The N,N-disubstituted hydroxylamines were prepared by treating *N*-benzylhydroxylamines[7] with the appropriate benzyl halide in the presence of sodium carbonate, according to the general directions of Behrend and Leuchs.[17] The preparation of *N*-*p*-methylbenzyl-*N*-benzylhydroxylamine is representative.

A mixture of 4.0 g (32.5 mmol) of *N*-benzylhydroxylamine and 4.55 g (32.5 mmol) of *p*-methylbenzyl chloride in 25 ml of 70% ethanol with 3.46 g (32.5 mmol) of sodium carbonate was refluxed with stirring for 4 hr. Cooling and dilution with 200 ml of ice–water caused an oil to separate, which was extracted with 200 ml of ether. Evaporation of the dried ($MgSO_4$) extract left 6.08 g (82.5%) of crude product. Recrystallization from aqueous ethanol gave 3.94 g (54%) of *N*-*p*-methylbenzyl-*N*-benzylhydroxylamine, mp 92–98°; an analytical sample, mp 96–99°, was prepared by recrystallization from ligroin (bp 90–100°); ir (Nujol mull) 3025–3150, 1520, 1500, 1360, 1105, 1080, 1035, 850, 815, 755, and 710 cm^{-1}; NMR δ 2.26 (s, 3 H), 3.64 (s, 4 H), 7.16 and 7.04 (m, total 9 H).

The results are recorded in Table I (the ir spectra, not being particularly informative, are omitted).

Oxidations. For a given oxidizing agent, the procedure was essentially the same for each hydroxylamine. A representative example for each oxidizing agent is described.

***N*-Bromosuccinimide Oxidations.** A solution of 0.30 g (1.17 mmol) of *N*-*o*-nitrobenzyl-*N*-benzylhydroxylamine in 20 ml of chloroform was added to a stirred, cooled solution of 0.2808 g (1.17 mmol) of *N*-bromosuccinimide and 0.09 g (1.17 mmol) of pyridine in 30 ml of chloroform. The mixture was stirred for 10 min and then washed with 50 ml of water. Evaporation of the dried ($MgSO_4$) and filtered chloroform layer under aspirator vacuum left 0.281 g (94%) of mixed nitrones.

Diacetoxyiodobenzene Oxidations. A solution of 0.378 g (1.17 mmol) of diacetoxyiodobenzene (phenyliodoso acetate) in 20 ml of methylene chloride was added dropwise to a cooled solution of 0.30 g (1.7 mmol) of *N*-*o*-nitrobenzyl-*N*-benzylhydroxylamine and 0.23 g (2.34 mmol) of cyclohexylamine in 30 ml of methylene chloride. The mixture was then stirred for 1–5 hr, washed with two 50-ml portions, dried ($MgSO_4$), and filtered. Evaporation of the solvent under aspirator vacuum left a mixture of nitrones with some iodobenzene, which did not interfere with NMR analysis and was not removed.

Mercuric Oxide Oxidations. A suspension of 1.0 g of mercuric oxide in 30 ml of ether containing 0.20 g (0.775 mmol) of *N*-*o*-nitrobenzyl-*N*-benzylhydroxylamine was stirred for 3 hr at ambient temperature. Monitoring by TLC analysis showed incomplete reaction. A further 1.0 g of mercuric oxide was added and the mixture was stirred for 3 more hr, but TLC still showed incomplete reaction. A third 1.0-g portion of mercuric oxide was added and the mixture was stirred for 2 hr and then filtered. Evaporation left 0.181 g (91%) of mixed nitrones.

Iodine Oxidations. A solution of 0.207 g (0.83 mmol) of iodine in chloroform was added over a period of 0.5 hr to a solution of 0.20 g (0.82 mmol) of *N*-*p*-methoxybenzyl-*N*-benzylhydroxylamine and 0.13 g (1.64 mmol) of pyridine in 50 ml of chloroform, and the mixture was stirred for 0.5 hr. Washing with three 50-ml portions of water removed the small amount of precipitate that had formed. Evaporation of the dried ($MgSO_4$) and filtered solution under aspirator vacuum left 0.198 g (99%) of mixed nitrones.

Oxidations by *tert*-Butyl Hydroperoxide. A solution of 0.30 g (1.21 mmol) of *N*-*p*-chlorobenzyl-*N*-benzylhydroxylamine and 0.117 g (1.3 mmol) of *tert*-butyl hydroperoxide in 5 ml of benzene was heated at 55° for 3 hr and then at gentle reflux for 21 hr (TLC showed that reaction was complete at that time). The solvent was removed under aspirator vacuum, and the residue was used directly for NMR assay.

Oxidation by Ceric Ammonium Nitrate. A solution of 0.2 g (0.81 mmol) of *N*-*p*-chlorobenzyl-*N*-benzylhydroxylamine in 40 ml of ether was shaken for 5 min with a solution of 0.89 g (1.62 mmol) of ceric ammonium nitrate in 40 ml of water. The ether layer was separated, washed with 50 ml of dilute sodium carbonate solution, dried ($MgSO_4$), and filtered. Removal of the solvent under aspirator vacuum left 0.184 g (93%) of mixed nitrones.

NMR Analysis. The mixtures of nitrones were dissolved in $CDCl_3$ containing a trace of triethylamine, and analyzed according to the method in the preceding paper.

Registry No.—*N*-*p*-Nitrobenzylhydroxylamine, 2912-97-2; *N*-*p*-chlorobenzylhydroxylamine, 51307-68-7; *N*-*p*-methylbenzylhydroxylamine, 16814-17-8; *N*-*p*-methoxybenzylhydroxylamine, 51307-59-6; *N*-*m*-nitrobenzylhydroxylamine, 55606-47-8; *N*-*m*-

methoxybenzylhydroxylamine, 55606-48-9; *N*-*o*-nitrobenzylhydroxylamine, 37558-77-3; *N*-*o*-chlorobenzylhydroxylamine, 55606-45-6; *N*-*o*-methoxybenzylhydroxylamine, 55606-46-7; α-bromotoluene, 100-39-0; α-chlorotoluene, 100-44-7; *p*-nitro-α-bromotoluene, 100-11-8; *N*-benzylhydroxylamine, 622-30-0; *p*-methylbenzyl chloride, 104-82-5; *N*-bromosuccinimide, 128-08-5; phenyliodoso acetate, 3240-34-4; mercuric oxide, 21908-53-2; iodine, 7553-56-2; ceric ammonium nitrate, 16774-21-3.

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Photochromism of Quinolylhydrazones. III.[1] The Mechanism of Isomerization of the Photocolored α-Quinolylimino-(*Z*)-hydrazone to the α-Quinolylamino-(*E*)-hydrazone

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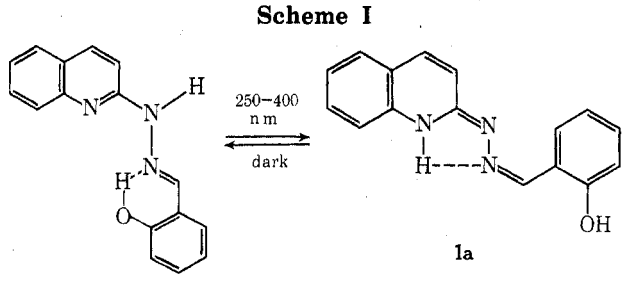
The kinetics and mechanism of the thermal decay of the photocolored form **1a** of salicylaldehyde 2-quinolylhydrazone (**1**) are reported. Two isomerization reactions, viz., α-imino- to α-aminoquinoline and $Z \rightarrow E$ hydrazone, are involved. The first conversion occurs via an intramolecular transfer of the phenolic hydrogen to the α-imino group. This is deduced on the basis of medium effect, concentration effect, and base inhibition studies. The decay of the 8-nitro colored form **2a** confirms this and implicates the quinoline NH as the source of the phenolic hydrogen of the uncolored form. The overall deuterium isotope effect of 1.84 denotes the non-rate-determining nature of the participation of the OH and NH. Since plots of the logarithm of the decay rate constant k vs. solvent Z or E_T (30) values show linear relationship and large negative $\Delta S^{\ddagger}$ values accompany the decay process, a rotation mechanism is postulated for the $Z \rightarrow E$ hydrazone isomerization. Also, acid catalysis substantiates the mechanistic scheme proposed for the decay process.

The photochromic phenomena of anils[2] and hydrazones[3] are generally observed only in a solid matrix. The instability of these colored forms in solution is typified by the *N*-salicylidene anil in the trans-quinonoid structure,[4] which showed a half-life of 1 msec at 30° in ethanol.[5a] The transient hydrazone photocolored species remains elusive. By contrast, the photochromism of salicylaldehyde 2-quinolylhydrazone (**1**) has been shown as follows (Scheme I).[1]

Scheme I



1 **1a**

The quinolylhydrazone **1** in ethanol is readily converted to the colored form **1a** when irradiated in the uv region of 250–400 nm at room temperature. This colored species has shown remarkable stability in both protic and aprotic solvents at room temperature. The availability and stability of **1a** thus afforded us an opportunity to investigate the relatively unexplored isomerization of α-heterocyclic imines and *Z* hydrazones. While *E,Z* isomerizations of the azomethine double bond in aldimines[5] and ketimines[6] have been the subjects of intensive studies, there is as yet no reported mechanism for the interconversions of hydrazones. This article details the kinetics and mechanisms of these isomerizations. The sequence of events reported herein also represents the first elucidated thermal decay process of the hydrazone photochromism.

Results and Discussion

Intramolecular Hydrogen Transfer. In the isomerization of **1a** to **1**, involving imine → amine and $Z \rightarrow E$ hydrazone conversions, one or more hydrogen transfer steps must intervene. They may occur inter- or intramolecularly as shown in Scheme II. Scheme IIa supposes a hydrogen transfer between **1a** and a protic solvent. That this is not generally applicable is shown by (1) the instant conversion of **1a** to **1** when the colored form is heated to its melting point at 152° in an evacuated sealed tube, and (2) the decay constant of **1a** to **1** at 25° in an aprotic medium such as dimethyl sulfoxide (1.2×10^{-6} sec^{-1}) is similar to that in ethanol (3.0×10^{-6} sec^{-1}). Scheme IIb assumes intermolecular transfer between adjacent molecules of **1a**. Such a mechanism should be facilitated by increasing concentrations of **1a**. However, when the decay of **1a** was followed in ethanol at 25°, varying the concentration of **1a** from 4×10^{-5} *M* to 20×10^{-5} *M* caused only negligible change in the first-order rate constant (k, 10^{-6} sec^{-1}, 2.11 and 2.0, respectively). A corollary observation was made in methylcyclohexane, a solvent which facilitates aggregation of solute molecules. In this case, the decay constant k (10^{-6} sec^{-1}, 25°) actually decreased from 2.56 at 0.5×10^{-5} *M* to 1.25 at