Kinetic and Molecular Orbital Studies on the Reaction of 5-nitrofurfural Hydrazone Formation

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Kinetic measurements of the 5-nitrofurfural-hydrazine reaction in various pH ranges of aquous solution were carried out by ultraviolet spectrophotometry at 25°, 35° and 45°C. the observed rate of the reaction varies with the change in pH, which gives characteristic "bell-type" rate acidity profile. The maximum rate is shown in the vicinity of pH 4. This reaction procceds with rate-determining attack of hydrazine on the 5-nitrofurfural at low pH and undergoes a change in rate-determining step to dehydration of the addition intermediate as pH increases. The reaction has a "reactant-like transition state" which precedes intermediate in low pH and "product-like transition state" which follows it in neutral pH. The geometry of 5-nitrofurfural-hydrazine intermediate was estimated with PCILO method associated with CNDO/2 scheme.

Introduction

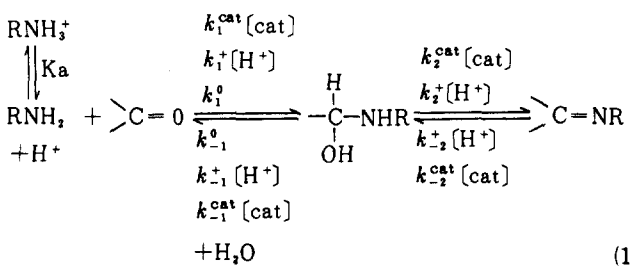
The condensation of amines with carbonyl compounds to yield imines proceeds by a stepwise mechanism involving formation of a tertrahedral addition intermediate followed by its dehydration to yield the observed product. The mechanism of many oxime, hydrazone, semicarbazone formation were studied.[1-5]

The observed rate of such a reaction varies with pH, giving a characteristic 'bell-type' rate-acidity profile. In general, this type of reaction proceeds with rate-determining attack of amine on the carbonyl compound at low pH and undergoes a change in rate-determining step to acid catalyzed dehydration of the tetrahedral addition intermediate as the pH is increased.[6-3]

Several investigations have established that the reactions of semicabazide with aldehydes and ketones are subject to general acid catalysis.[7,9,10] The general acid-catalyzed reaction of substituted hydrazines with p-chloro-benzaldehyde was studied by J.M. Sayer *et al.*[11]

The present investigation was carried out in an attempt to determine the geometry of carbinolamine intermediate. We studied the reaction of 5-nitrofurfural and hydrazine kinetically and from the kinetic data, we determined the geometry of reaction intermediate theoretically using PCILO method.

The overall reaction scheme is of the form.[9]



(1)

At zero buffer concentration the contributions of k_1^{cat} [cat], k_{-1}^{cat} [cat], k_2^{cat} [cat] can be omitted. In the case that the dehydration step is rate determining step, the rate of the overall reaction is expressed as follows.

$$\frac{d[\succeq C=NR]}{dt} = (k_1^{\circ}+k_1^{+}[H^+])[\succeq C=O][RNH_2] - (k_{-1}^{\circ}+k_{-1}^{+}[H^+])[-\underset{OH}{\overset{H}{C}}-NHR]+k_2^{+}[H^+][-\underset{OH}{\overset{H}{C}}-NHR] \quad (2)$$

where, $[\succeq C=O]$, $[RNH_2]$ and $[-\underset{OH}{\overset{H}{C}}-NHR]$ are the concentration of aldehyde, free amine base, carbinolamine intermediate, respectively. The rate of carbinolamine formation is expressed by

$$\frac{d[-\underset{OH}{\overset{H}{C}}-NHR]}{dt} = (k_1^{\circ}+k_1^{+}[H^+])[\succeq C=O][RNH_2] - (k_{-1}^{\circ}+k_{-1}^{+}[H^+]) \times [-\underset{OH}{\overset{H}{C}}-NHR] - k_2^{+}[H^+][-\underset{OH}{\overset{H}{C}}-NHR] \quad (3)$$

At steady state the rate of intermediate formation is zero

$$\frac{d[-\underset{OH}{\overset{H}{C}}-NHR]}{dt} = 0 \quad (4)$$

Then using eq.(3) and eq.(4) we can obtain the concentration of carbinolamine intermediate.

$$[-\underset{OH}{\overset{H}{C}}-NHR] = \frac{(k_1^{\circ}+k_1^{+}[H^+])[\succeq C=O][RNH_2]}{k_{-1}^{\circ}+k_{-1}^{+}[H^+]+k_2^{+}[H^+]} \quad (5)$$

Substituting eq.(5) into eq.(2) we obtain the following relationship

$$\frac{d[\succeq C=NR]}{dt} = [\succeq C=O][RNH_2]\left\{k_1^{\circ}+k_1^{+}[H^+] - \frac{(k_{-1}^{\circ}+k_{-1}^{+}[H^+]-k_2^{+}[H^+])(k_1^{\circ}+k_1^{+}[H^+])}{k_{-1}^{\circ}+k_{-1}^{+}[H^+]+k_2^{+}[H^+]}\right\}$$

$$= [\succeq C=O][RNH_2](k_1^{\circ}+k_1^{+}[H^+])$$

$$\frac{2k_2^+[H^+]}{k_{-1}^\circ+k_{-1}^+[H^+]+k_2^+[H^+]} \quad (6)$$

The rate expression of the overall reaction is also given by

$$\frac{d[\geq C=NR]}{dt}=k_2[\geq C=O][RNH_2] \quad (7)$$

where k_2 is the second order rate constant of the reaction.

If we maintain the concentration of amine greatly in excess of that of the aldehyde, the pseudo first-order kinetics were obtained.

$$\frac{d[\geq C=NR]}{dt}=k_{obs}[\geq C=O] \quad (8)$$

Comparing eq.(6) with eq.(8) we obtain the next equation.

$$k_2=\frac{2(k_1^\circ+k_1^+[H^+])k_2^+[H^+]}{k_{-1}^\circ+k_{-1}^+[H^+]+k_2^+[H^+]} \quad (9)$$

Using the relationship,

$$K_1=\frac{k_1^\circ}{k_{-1}^\circ}=\frac{k_1^+}{k_{-1}^+} \quad (10)$$

where K_1 is the formation constant of carbinolamine, we rewrite eq.(9) as follows.

$$k_2=\frac{k_{obs}}{[RNH_2]}=\frac{2k_2^+K_1[H^+](k_1^+[H^+]+k_1^\circ)}{k_1^\circ+k_1^+[H^+]+k_2^+ +K_1[H^+]} \quad (11)$$

Therefore, the overall rate constant k_2 can be clculated from dividing k_{obs} by the concentration of free amine base and represented by the second relationship in eq.(11).

Experimental

Materials. 5-nitrofurfural was redistilled and stored in the cold. Stock solution of 5-nitrofurfural was prepared in ethanol and was stored at 4°C. This was diluted on the day of use with water containing sufficient ethylenediaminetetraccetic acid (EDTA) to give a concentration of 10^{-4} M in the final reaction mixture. The EDTA was used to retared heavy metal catalyzed decomposition. The ethanol concentration in the final reaction mixtures was less than 0.2%.

Hydrazine solutions were made by dissoving the free base in water. Glass-distilled water was used throughout.

Kinetic measurements. were made on SHIMADZU-210A spectrophotometer with jacketed cell compartments through which was circulated water from a thermostat at 25°C, 35°C and 45±0.1°C.

buffers containing hydrazine and potassium chloride to maintain the ionic strength of 1.0 were adjusted to a given pH using sodium hydroxide solution. Measurements of pH were made with glass electrode and the Fisher Accumet pH meter Model 292. The 3.0 *ml* of buffer solution was then placed in a cuvette and equilibrated in the cell compartment of a spectrophotometer. 5-nitrofurfural in water was added via a lambda pipette. Readings were taken beginning 10 to 15 seconds after the start of the reaction and continued, usually with about 10 readings, until the reaction has proceeded to completion.

All kinetic determinations were carried out with the concentration of hydrazine greatly in excess of that of the 5-nitrofurfural so that pseudo first-order kinetics were obtained. Good first-order plots were usually obtained. The absorptions at time zero of the reactions were calculated by extrapolating the first-order polots to zero time. Spectral data for the reactants and product and the conditions used in the kinetic experiments are summarized in Table 1. Rates were followed at a wavelength, as indicated in the experimental data, suitable for measurements of product appearance or, after the initial rapid drop, of starting material disappearance. Pseudo first order rate constants of the reaction were determined from semilogarithmic plot of (A_∞-A_t) against time.

Calculation

1. PCILO Method. PCILO[12] (Pertubation Configuration Interaction using Localized Orbitals) was born during the study of the pertubation treatment of configuration interaction using SCF localized orbitals. PCILO is specially fitted for conformation analysis.

2. Application. We calculated the total energies of the molecules using computer program[13] based on PCILO theory.

Examination of the geometry of the intermediate is the main

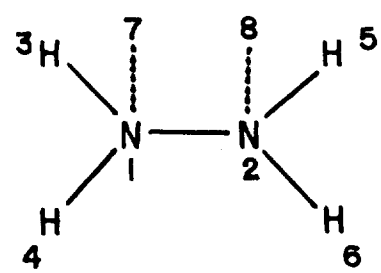


Figure 1. Choice of an absolute numbering.

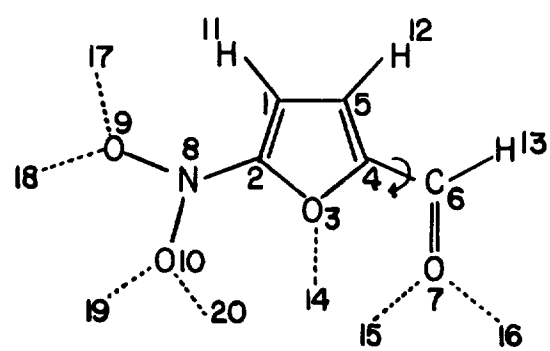


Figure 2. Choice of an absolute numbering.

TABLE 1: Experimental Conditions[a] for Determination of rate Constants for 5-nitrofurfural Hydrazone Formation

Compound		Type	Concn., M		max, nm		
Aldehyde	Amine	expt.	Aldehyde	Amine	Aldehyde	Amine	Product
5-nitro-	Hydrazine	first		0.09			383[b]
			8×10^{-5}	0.054	310	204	
furfural		order		0.018			384

[a]Kinetic experiments at 25°, 35°, 45°C and ionic strength 1.0 [b]at pH 7.54.

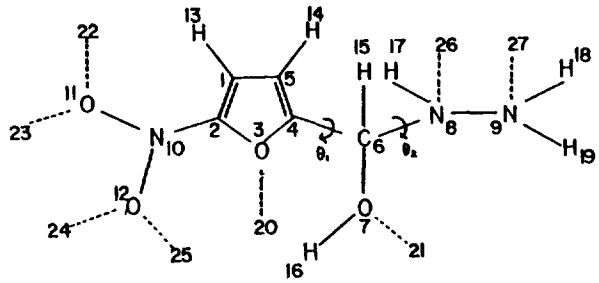


Figure 3. Choice of an absolute numbering.

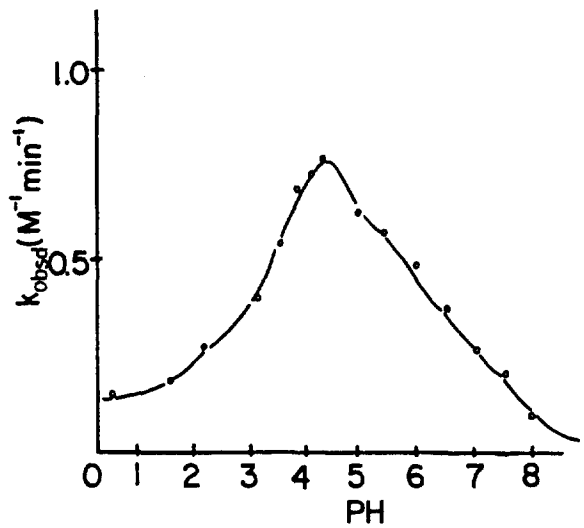


Figure 4. Rate of reaction of 5-nitrofurfural with hydrazine as a function of pH: 8×10^{-3}M 5-nitrofurfural, 0.054M hydrazine, ionic strength maintained at 1.0 with KCl, measured at 310nm. All rate constants have been extrapolated to zero buffer concentration.

purpose.

We give absolute numbers to the atoms in the molecules. The heavy atoms first, then the hydrogen atoms and finally the fictitious atoms, introduced in the direction of the lone pairs. (Figure 1-3) Then we define a treestructure on the molecule. The data needed for calculation is all bond lengths and bond angles included in the tree-structured molecule. The geometries of molecules we used as input data are as follows.

(1) Hydrazine

From the literature we have taken the geometry of hydrazine as Figure 1. The dotted lines in Figure 1 represent lone pair electrons.

(2) 5-nitrofurfural

We obtained the geometrical data of 5-nitrofurfural from literature and represented in Figure 2. In this molecule, we calculated the total energies for the two conformations *cis*- and *trans*- which are differing in dihedral angle between furan ring and aldehyde group.

(3) 5-nitrofurfural-hydrazine intermediate

As the geometry of carbinolamine was known to be tetrahedral, we assumed the geometry of 5-nitrofurfural-hydrazine intermediate as follows.

In Figure 3, Θ_1 and Θ_2 are dihedral angles between furan ring and aldehyde group, aldehyde group and hydrazine molecule, respectively.

We considered various conformations differing in Θ_1 and Θ_2. We calculated the total energies for the eight extreme conformations of this intermediate. That is, $\Theta_1=0°$ and 180°, $\Theta_2=0°$, 90°, 180° and 270°. We also determied the listance of bond C-N which was newly formed in the reaction intermediate.

TABLE 2: Equilibrium and Apparent Rate Constants for the Reaction of 5-nitrofurfural with Hydrazine

K_{12}	2.37×10^{6}
K_1	14.92
K_2	1.59×10^{5}
k_0^1	7.6×10^{4}
k_+^1	2.44×10^{8}
k_0^{-1}	5.09×10^{3}
k_+^{-1}	1.64×10^{7}
k_+^2	3.67×10^{7}
k^{+2}	2.31×10^{2}

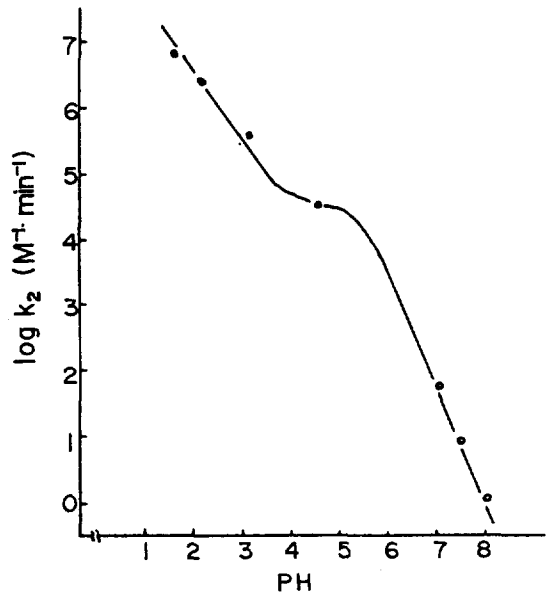


Figure 5. Dependence on pH of the logarithms of second-order rate constants, based on the concentration of hydrazine free base, 5-nitrofurfural hydrazone formation at 25°C, ionic strenght 1.0. All rate constants have been extrapolated to zero buffer concentration.

Result and Discussion

1. Kinetics. The rate of 5-nitrofurfural hydrazone formation is increased by buffer. This acceleration suggests that this reaction is subject to general acid catalysis by buffer acid as well as to specific acid cataysis. If we evaluate the values of rate constants at zero buffer concentration we obtain the dependence on pH of the rate constants for 5-nitrofurfural hydrazone formation and the result is shown in Figure 4.

The pH-rate curve is similar to those observed for semicarbazone and oxime formation.[1-5] The break in the curve at about pH 4.5 is indicative of a change from rate-determining addition of the nucleophile at low pH to rate-determining dehydration of the addition intermediate at higher pH. The addition step proceeds through both an acid-catalyzed and a pH-independent pathway, while dehydration is predominantly acid catalyzed.[6-8]

Second-order rate constant of this reaction, obtained by dividing the observed pseudo first-order rate constant by the concentration of free hydrazine, is plotted logarithmically in

TABLE 3: Thermodynamic Parameters for the Reactions of 5-nitrofurfural with Hydrazine at 25°C

pH	2.19	8.03
ΔH‡ (kcal)	8.58	11.94
ΔG‡ (kcal)	11.14	19.46
ΔS‡ (e.u)	−8.57	−25.22

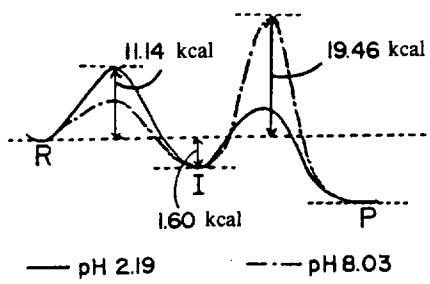


Figure 6. The reaction profile of 5-hitrofurfural-hydrazine. (R: Reactant I: Intermediate P: Product)

TABLE 4: The Total Energies and Dipole Moments of 5-nitrofurfural and Hydrazine Calculated by PC1L0 Method

Rotation axis	Ring-C	Hydrazine	5-nitrofurfural 0.0	5-nitrofurfural 180.0
E_{total}		−16,521.246	−72,355.625	−72,351.812
Dipole moment		0.0001D	11.1252D	17.0574D

Figure 5 as a function of pH.

We evaluated the formation constants and rate constants for all of the steps of this reaction and the results are listed in Table 2.

Using the following fundamental equations we also estimated thermodynamic parameters at some pH. (Table 3)

$$\ln(k_2/T) = -\frac{\Delta H^*}{R}\cdot\frac{1}{T} + \text{const} \quad (12)$$

$$\Delta G^* = -RT\ln\frac{hk_2}{kT} \quad (13)$$

$$\Delta S^* = (\Delta H^* - \Delta G^*)/T \quad (14)$$

From the fact that the reaction enthalpy is relatively small and the activation entropy is negatively large, we can say that this reaction is S_N 2. Th absolute value of activation entropy is larger at neutral pH than at acidic pH and this is due to the fact that at neutral pH the adition intermediate is hard to dehydrate.

We can also obtain the reaction profile of 5-nitrofurfural hydrazone formation using thermodynamic parameters (Table 3) and formation constants (Table 2). The result is illustrated in Figure 6.

2. PCILO Calculation. The energies and dipole moments were computed for several assumed spatial geometries of each species. The results of PCILO calculation for the reactants, 5-nitrofurfural and hydrazine, are summarized in Table 4.

Table 4 showes that, in the two conformations of 5-nitrofurfural, the *cis*-form is more stable than the trans-form.

TABLE 5: The Total Energies and Dipole Moments of various Conformations of 5-nitrofurfural-hydrazine Intermediate Calculated by PCILO Method (C-N bond length: 1.269 A)

Conformation		*A*	*B*	*C*	*D*
Rotation axis	Ring-C	0.0	180.0	0.0	180.0
	C-N	0.0	0.0	90.0	90.0
E_{total}		−88,898.875	−88,900.750	−88,841.562	−88,841.375
Dipole moment		15.3515D	10.8247D	14.4718D	16.5669D
			( )		
Conformation		*E*	*F*	*G*	*H*
Rotation axis	Ring-C	0.0	180.0	0.0	180.0
	C-N	180.0	180.0	270.0	270.0
E_{total}		−88,750.687	−88,749.812	−88,779.187	−88,782.187
Dipole moment		20.086D	22.6750D	20.5313D	19.4267D

So we chose the geometry of 5-nitrofurfural as *cis*-from. Then the sum of the total energies of reactants is−88,876.871 kcal (−16,521.264 Kcal −72,355.625 kcal) and from the reaction profile shown in Figure 6 we know that the energy difference between the reactants and intermediate is 1.60 kcal. Accordingly, we can infer that the total energy of 5-nitrofurfural-hydrazine intermediate is −88,878.471 kcal.

In the reaction intermediate, we calculated the total energies for the eight conformation differing in two dihedral angles Θ_1 and Θ_2 and found that conformation B ($\Theta_1 = 180$, $\Theta_2 = 0$) is most stable. Then we proceeded further calculation for this conformation B in order to find the optimum C-N bond length.

The closest value of total energy to the experimentally estimated value (−88,878.471 kcal) is obtained when C-N bond distance is 1.269 A. The results are shown in Table 5.

Concludingly, the geometry of 5-nitrofurfural-hydrazine intermediate is the trans form of Figure 3 in which the dihedral angle Θ_1 is 180° and the C-N bond distance is 1.269 A.

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Quantitative Determination of Acetone formed in the Thermal and Photochemical Decompositions of Azobisisobutyronitrile

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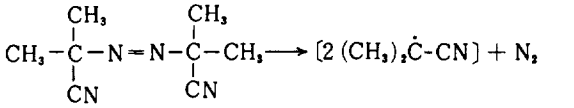
Cyanoisopropyl radical derived from azobisisobutyronitrile (AIBN) by either thermolysis or photolysis reacts with oxygen to give cyanoisopropylperoxy radical which then was converted to acetone and cyano radical and/or acetyl cyanide and methyl radical. Of these products, acetone formed was quantitatively determined by the addition of thianthrene cation radical perchlorate to the reaction mixture. The results showed that 55.7 mmol, 16.9 mmol, and 16.0 mmol of acetone were formed for 7 hours from 1 mol of AIBN at 82±1°C in acetonitrile, carbon tetrachloride, and benzene, respectively. However, 22.2 mmol of acetone was formed from photolysis of 1 mmol of AIBN in acetonitrile. The value decreased to 13.2 mmol by bubbling argon into the solvent prior to photolysis.

Introduction

Thermal decomposition of AIBN under a degassing condition produces cyanoisopropyl radicals in pair, which then undergo a variety of reactions as shown in the following equations.



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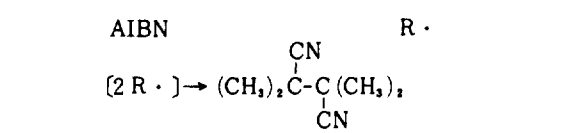

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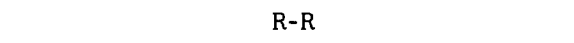

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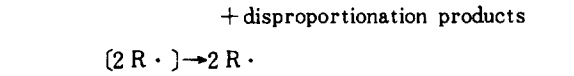
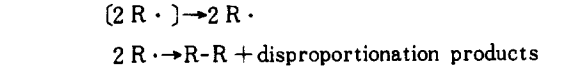


(4)

The coupling product, tetramethylsuccinonitrile (R-R) is formed in the solvent cage or outside of the solvent cage as shown in eqs. (2) and (3), respectively. In the meantime, cyanoisopropyl radical is scavenged efficiently by oxygen molecule. The peroxy radicals thus formed have been reported to immediately become hydroperoxide and other products (eqs. 5,6)[1,2] whose pathways strongly depended on the hydrogen atom donor.



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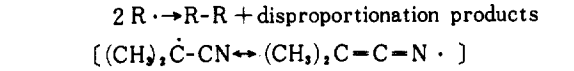
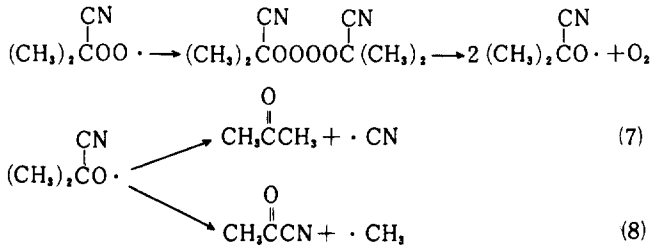


(6)

In the case of the absence of good hydrogen atom donor, it is expected that cyanoisopropylperoxy radical undergoes different reactions.[3] By the analogy with the cleavage mode of *t*-butylperoxy radical,[3] two kinds of cleavage reactions appear in mind. That is, dimerization, followed by the extrusion of oxygen molecule to give cyanoisopropoxy radical which then undergoes α scission to give either acetone and cyano radical (eq. 7) or acetyl cyanide and methyl radical (eq. 8).



(7)

(8)

To our knowledge, no such investigation on cyanoisopropylperoxy radical has been made. In order to determine quantitatively the amount of acetone formed was used thianthrene cation radical perchlorate which has been reported to react quantitatively with acetone to give 5-acetonylthianthrenium perchlorate.[5]

Experimental

AIBN was from Merck and was recrystallized from absolute ethanol. Thianthrene and thianthrene cation radical perchlorate were prepared by the methods described elsewhere.[6] Acetonitrile was Kanto Chemical Corporation Extra Pure and was refluxed with phosphorus pentoxide for three hours. By redistilling the first distillate was obtained dried acetonitrile. Nitrogen and argon gases were purchased from Korea Helium Company. The former was dried by passage through calcium chloride tube, followed by conc. sulfuric acid and the latter was passed through Hydrox Purifier (Mallinckrodt, Model No. 8301) to remove oxygen completely.

Column chromatography was performed with Merck silica