

Kinetics of the Base-Catalyzed Decomposition of α -Hydroperoxy Nitriles. Chemiluminescence and Dioxetanimine Mechanism

Yasuhiko Sawaki and Yoshiro Ogata*

Contribution No. 236 from the Department of Applied Chemistry,
Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya 464, Japan.
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Abstract: Base-catalyzed decomposition of α -hydroperoxy nitriles $R_1R_2C(OOH)CN$, **1**, has been studied kinetically in MeOH or water and chemiluminescence is observed by addition of a suitable fluorescer. The reaction with 0.1 M MeONa is completed within 2 h at 25 °C, affording 75–100% yields of ketones, $R_1R_2C=O$, and OCN^- . The reaction satisfies first-order kinetics with respect to **1** and the rate constant increases with increasing pH, approaching a constant value at pH >12. The pK_a value of **1a** ($R_1 = R_2 = Me$) from the pH-rate profile is 10.9 in water, which is close to the value of 11.3 determined from the UV absorbance. Cyanide ion is not produced and the addition of CN^- has no effect either on the rate or products. Introduction of one phenyl group accelerates the rate by a factor of 15. The addition of dibromoanthracene to the reaction mixture leads to weak chemiluminescence ($\Phi = 4 \times 10^{-8}$ to 3×10^{-6}). Inefficiency of diphenylanthracene indicates predominant formation of triplet ketone. These results are explained by a cyclic mechanism containing a rate-determining fragmentation of dioxetanimine **3**.

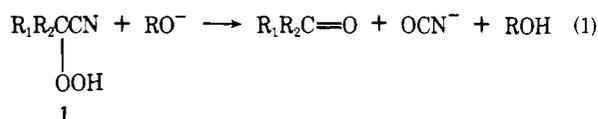
Base-catalyzed autoxidation of nitriles is known to give ketones by oxidative decyanation^{1,2} and intermediary α -hydroperoxy nitriles (**1**) have been isolated in some cases.^{2–4} A cyclic mechanism has been written for the base-catalyzed decomposition of the hydroperoxide without any mechanistic study.⁵ Here, we wish to report our kinetic study on the base-catalyzed decomposition of **1a–e** which accompanies weak chemiluminescence in the presence of a suitable fluorescer.

Recently, we reported that an intramolecular acyclic fragmentation is a predominant pathway for the base-catalyzed decomposition of α -hydroperoxy ketones⁶ and esters,⁷ a minor one being a cyclic chemiluminescent decomposition. The present alkaline reaction of **1** seems, in contrast to these cases, to proceed via the unimolecular cyclic mechanism similar to the case of α -hydroperoxy chloride.⁸

Results and Discussion

α -Hydroperoxy nitriles ($R_1R_2C(OOH)CN$, **1**) were synthesized by *t*-BuOK-catalyzed autoxidation of substituted acetonitriles at –60 °C. The crude peroxides could be purified by passing them through Florisil since the peroxides are sensitive to base but are stable under acidic conditions.

Products. The decomposition of **1** with 0.10 M MeONa was completed within 30 min for aromatic peroxides **1b–e** and 2 h for **1a**, affording ketones and cyanate ion (eq 1, $R = H$ or Me).



The yields of ketones are high (75–100%) as shown in Table I, and cyanide ion was not detected for all cases by benzidine-cupric acetate test.⁹ Quantitative formation of cyanate ion has been reported for the case of **1a**.⁴

Rates. The base-catalyzed decomposition of **1** was monitored up to 80% conversion by iodometry and found to obey satisfactorily first-order kinetics with respect to **1**, which was not changed by varying initial concentrations (Table IIB).

$$v = k_{\text{obsd}}[\mathbf{1}] \quad (2)$$

The reactivities of various **1** (R_1, R_2) are in the order **1a** (Me, Me) \ll **1d** (Ph, Et), **1e** (Ph, Me) $<$ **1c** (Ph, PhCH₂) \ll **1b** (Ph, Ph). The substitution of one phenyl accelerates the decomposition by a factor of ca. 15; the peroxide **1b** decomposes 270

times as fast as **1a**. The effect of temperature is quite similar for all peroxides (ca. 30-fold increase in rate by 25 °C raise), suggesting similar values of activation energy.

Detailed kinetics were studied for the decomposition of **1a** in water (Table II). The peroxide is stable even in the presence of 2.5 M perchloric acid at 25 °C. The decomposition rate increases with increasing pH and approaches a constant value at higher pH (i.e., pH >12). Catalysis by carbonate or phosphate ion was not significant, since the rate was identical within experimental error when the buffer concentration was duplicated. The rate was not affected by the absence or the presence of EDTA, which suggests no intervention of metal-catalyzed decomposition of **1**.

The temperature effect was studied for **1a** at pH 13, where the rate is independent of base concentration (Table IIC). The resulting activation parameters are $\Delta H^\ddagger = 19.0$ kcal/mol and $\Delta S^\ddagger = -8.9$ eu, which are comparable with the case of base-catalyzed cyclization of $Me_2C(OOH)CH_2Cl$, i.e., $\Delta H^\ddagger = 24.4$ kcal/mol and $\Delta S^\ddagger = -10$ eu.⁸ The decomposition rate was practically identical even when solvent water was replaced by MeOH (Table IID). This is in sharp contrast with the decomposition of α -hydroperoxy ketones⁶ and esters,⁷ where the rate is much higher in water since the decomposition proceeds via the intermolecular addition of HO^- to $C=O$.

Cyanide ion is known to be oxidized to cyanate ion by hydroperoxides at over 50 °C.¹⁰ The addition of CN^- to the present reaction mixture at 25 °C, however, had no effect on the rate and cyanide was recovered quantitatively (Table IIB).

Chemiluminescence. Chemiluminescence was observed on addition of dibromoanthracene (DBA) but diphenylanthracene (DPA) was of no effect. This large difference in fluorescer efficiencies is well known in the thermolysis of dioxetanes and explained as a predominant formation of triplet ketone ($^3C=O$).^{11,12} Similarly, $^3C=O$ is produced chiefly from base-catalyzed decomposition of α -hydroperoxy ketones.¹³ The present reaction of **1** also suggests a primary formation of triplet ketone and $^3C=O/{}^3C=O$ is over 100 according to the reported analysis.^{11a}

The quantum yields from **1** and DBA are 4×10^{-8} to 3×10^{-6} (Table III) and hence the chemiluminescent system is not an efficient one. The rate constant from the decrease of the luminescence intensity of **1e** and DBA is approximately $1.2 \times 10^{-2} s^{-1}$ which is close to the value ($1.43 \times 10^{-2} s^{-1}$) by iodometry. The intensity of luminescence from other peroxides was insufficient for a measurement of the accurate rate.

Table I. Products and First-Order Rate Constants for the Base-Catalyzed Decomposition of α -Hydroperoxy Nitriles in MeOH^a

| | $R_1R_2C(OOH)CN$ | | Products, % ^b $R_1R_2C=O$ | $10^3 k_{obsd}$, s ⁻¹ | |
|-----------|------------------|-------------------|---|-----------------------------------|--------|
| | R_1 | R_2 | | 25.0 °C | 0.0 °C |
| 1a | Me | Me | 75 ^d | 0.866 | 0.0315 |
| 1b | Ph | Ph | 103 | >100 | 8.48 |
| 1c | Ph | PhCH ₂ | 100 | 25.6 | 0.810 |
| 1d | Ph | Et | 99 | 14.8 | 0.517 |
| 1e | Ph | Me | 95 | 14.3 | 0.548 |

^a Reaction with 0.02 M **1** and 0.1 M MeONa in MeOH. ^b Reaction at 25 °C for 30 min and ketones were estimated by GLC analysis unless otherwise noted. Cyanide ion could not be detected for all runs. Cyanate ion was not determined. ^c Averged first-order rate constants from two or three determinations. ^d Acetone was determined as 2,4-dinitrophenylhydrazone after the reaction with 0.1 M NaOH in water for 3 h.

Table II. Rates for the Base-Catalyzed Decomposition of $Me_2C(OOH)CN$ (**1a**) under Various Conditions

| Conditions ^a | pH | $10^3 k_{obsd}$, s ⁻¹ |
|---|-------------------|-----------------------------------|
| A. Effect of pH ^c | | |
| 2.5 M HClO ₄ | | <10 ⁻⁵ |
| 0.1 M HClO ₄ | 1.0 | <10 ⁻⁵ |
| 0.1 M KH ₂ PO ₄ | 4.5 | <10 ⁻⁵ |
| 0.1 M Na ₂ HPO ₄ -KH ₂ PO ₄ (1:1) | 6.8 | 0.00018 |
| 0.1 M NaHCO ₃ | 8.5 | 0.0082 |
| 0.1 M Na ₂ CO ₃ -NaHCO ₃ (1:1) | 10.6 | 0.218 |
| 0.1 M Na ₂ CO ₃ | 11.2 | 0.562 |
| 0.1 M NaOH | 13.0 | 0.836 |
| 0.2 M NaOH | 13.3 | 0.865 |
| B. Effect of [1a] and NaCN | | |
| 0.005 M 1a | 11.2 ^d | 0.534 |
| 0.01 M 1a | 11.2 ^d | 0.562 |
| 0.01 M 1a + 0.01 M NaCN ^e | 11.2 ^d | 0.570 |
| 0.03 M 1a | 11.1 ^d | 0.512 |
| C. Effect of Temperature | | |
| 25.0 °C | 13.0 ^f | 0.836 ^g |
| 15.0 °C | 13.0 ^f | 0.270 ^g |
| 0.0 °C | 13.0 ^f | 0.0404 ^g |
| D. Effect of Solvent | | |
| 0.1 M NaOH in H ₂ O | | 0.836 |
| 0.1 M NaOH in 50% MeOH | | 0.975 |
| 0.1 M MeONa in 100% MeOH | | 0.866 |

^a Reaction with [**1a**] = 0.01 M and [EDTA] = 5 × 10⁻⁴ M in water at 25.0 °C unless otherwise noted. ^b Means of two or three determinations (±5%). ^c Data for other pHs are also determined and plotted in Figure 1. The concentration of buffers is 0.1 M. ^d Reaction with 0.1 M Na₂CO₃. ^e Cyanide ion was not consumed after the reaction of **1a**. The concentration of CN⁻ was titrated with iodine in aqueous Na₂CO₃-NaHCO₃ buffer (1:1). ^f Reaction with 0.1 M NaOH. ^g Activation parameters: $E_a = 19.6$ kcal/mol, $\Delta S^\ddagger = -8.9$ eu.

Mechanism. Radical decomposition of **1** is unlikely since the rate constants were not altered by changing initial concentration of **1** or by the absence of EDTA and no product from benzyl radical was obtained from **1c** ($R_2 = PhCH_2$).¹⁴ Three pathways are conceivable, Schemes I-III, where RO⁻ is HO⁻ or MeO⁻.

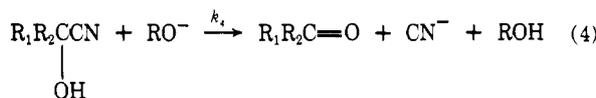
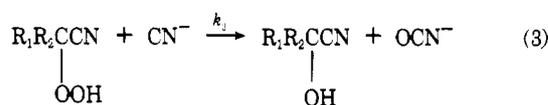
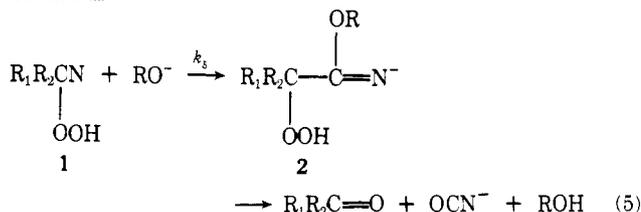
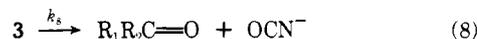
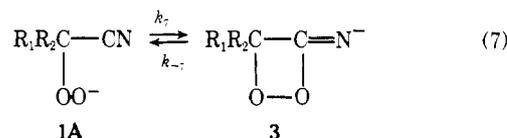
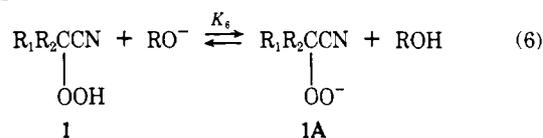
Base-catalyzed elimination of CN⁻ from cyanohydrin (eq 4) is very fast and hence Scheme I is possible if the reaction of **1** with CN⁻ has a considerable rate. The CN⁻ ion is known to be oxidized to OCN⁻ by hydroperoxides above 50 °C.¹⁰ But no reaction of **1** with CN⁻ occurs under the present conditions. These facts deny Scheme I.

Concerted fragmentations of C-C and O-O bonds such as **2** in Scheme II are well known for decompositions of peroxides, e.g., α -peroxy ketones,⁶ esters,^{7,16} acid,¹⁷ and alcohol.¹⁸

Table III. Chemiluminescence from the Base-Catalyzed Decomposition of **1** in MeOH at 25 °C^a

| Peroxide (R_1, R_2) | Fluorescer (Φ_F^A) ^b | Initial I^c | $10^6 \Phi_{CL}^d$ |
|------------------------------------|--|---------------|--------------------|
| 1a (Me, Me) | DPA (0.85) | 0 | 0.0 |
| | DBA (0.11) | 6 | 3.0 |
| 1e (Ph, Me) | DPA (0.85) | 0 | 0.0 |
| | DBA (0.11) | 11 | 1.0 |
| 1d (Ph, Et) | DBA (0.11) | 0.6 | 0.5 |
| 1c (Ph, PhCH ₂) | DBA (0.11) | 0.4 | 0.2 |
| 1b (Ph, Ph) | DBA (0.11) | ~0.3 | ~0.04 |

^a Reaction with [**1**] = 0.01 M, [fluorescer] = 2.5 mM, and [MeONa] = 0.12 M. ^b Fluorescence quantum yield under the reaction conditions from ref 7; DPA = diphenylanthracene and DBA = dibromoanthracene. ^c Relative intensity of initial chemiluminescence immediately after mixing reactants. ^d The quantum yields of chemiluminescence were calculated by the equation $\Phi_{CL} = I/(k_{obsd}[1] \times 6 \times 10^{23} \Phi_F^A)$. See ref 7 for details.

Scheme I**Scheme II****Scheme III**

Scheme II can explain the pH-rate profile only if the intermolecular addition of HO⁻ to C≡N is sufficiently fast. However, the addition of HO⁻ to nitriles is considerably slow; e.g., the second-order constant is 9.2 × 10⁻⁵ M⁻¹ s⁻¹ for *p*-O₂CC₆H₄CN¹⁹ and 1.59 × 10⁻⁶ M⁻¹ s⁻¹ for MeCN²⁰ in water at 25 °C. On the other hand, the observed rate constant of **1** with 0.1 M alkali ($k_{obsd} = 10^{-3}$ - 10^{-1} s⁻¹) necessitates the k_5 value to be over 10⁻² M⁻¹ s⁻¹. This large discrepancy denies Scheme II.

Alternatively, a pathway is also conceivable which contains the addition of peroxide anion **1A** to **1**, i.e., **1A** in place of HO⁻ in Scheme II. In fact, the reaction of HOO⁻ with nitriles is considerably fast, e.g., 0.11 M⁻¹ s⁻¹ for *p*-O₂CC₆H₄CN¹⁹ and 6.6 × 10⁻³ M⁻¹ s⁻¹ for MeCN²¹ in water at 25 °C.

Table IV. Properties and Spectra of α -Hydroperoxy Nitriles

| 1 (R ₁ , R ₂) | Mp, °C | Purity, % | IR (film), ^b cm ⁻¹ | | NMR, ^c δ |
|--------------------------------------|--------|-----------|---|-----|--|
| | | | C≡N | O-O | |
| 1a (Me, Me) | Liquid | 95 | 2230 | 845 | 1.62 (s, two CH ₃), 9.3 (s, OOH) |
| 1b (Ph, Ph) | 88-89 | 97 | 2240 w | 843 | 7.43 (s, two Ph), 8.90 (s, OOH) |
| 1c (Ph, PhCH ₂) | 92-94 | 100 | | 842 | 3.17, 3.43 (two d, <i>J</i> = 14 Hz, PhCH ₂), 6.9-7.4 (m, two Ph), 8.96 (s, OOH) |
| 1d (Ph, Et) | 71-72 | 102 | 2220 w | 840 | 1.0 (t, <i>J</i> = 7.5 Hz, CH ₃), 1.75-2.48 (m, -CH ₂ -), ^d 7.2-7.6 (m, Ph), 8.86 (s, OOH) |
| 1e (Ph, Me) | Liquid | 86 | 2240 w | 850 | 1.83 (s, CH ₃), 7.3-7.6 (m, Ph), 9.84 (s, OOH) |

^a Determined iodometrically. ^b Strong, broad peak of OOH is also observed at 3310-3330 cm⁻¹. ^c The δ values vs. Me₄Si in CCl₄ for 1a,e and CDCl₃ for 1b,c,d. Peak areas were consistent with the number of protons of the indicated group. ^d Presumably, δ 2.03, 2.13 (two q, *J* = 7.5 Hz, CH₂).

However, this pathway necessitates second-order dependency of the rate on **1**, which is not the case.

On the other hand, all the results may be explained by Scheme III as stated below.

(1) Scheme III can explain the observed pH-rate profile of **1a**. That is, the observed data (k_{obsd}) for **1a** can be well reproduced by assuming $\text{p}K_{\text{a}} = 10.9$ and $k_1 = 0.87 \times 10^{-3} \text{ s}^{-1}$ as a first-order rate constant of the decomposition of **1A** (see Figure 1). The $\text{p}K_{\text{a}}$ value from the kinetics is close to the value ($\text{p}K_{\text{a}} = 11.3$) from UV absorbance in water at 23 °C.²²

(2) Observation of chemiluminescence coincides with the decomposition via a dioxetanamine **3**.

(3) Neighboring group participations are well known²³ and the related intramolecular four-membered ring formation is 10^2 - 10^3 times as fast as the intermolecular reaction.⁸ The rate constant for the intermolecular addition of HOO⁻ is ca. $10^{-2} \text{ M}^{-1} \text{ s}^{-1}$ for nitriles such as MeCN and PhCH₂CN in 50% MeOH at 25 °C.²¹ These values are of similar magnitude with the decomposition rate of **1** (10^{-2} - 10^{-3} s^{-1}), suggesting that the rate-determining step is not the intramolecular cyclization (eq 7) but the fragmentation of dioxetanamine **3** (eq 8). That is, if eq 7 is a slow step, it is difficult to explain why the neighboring group acceleration is absent for the cyclization of **1A** while a large acceleration is observed in the dioxetane formation from Me₂C(OO⁻)CH₂Cl.⁸

(4) Significant solvent effect is observed for the base-catalyzed epoxide formation from chlorohydrin and the reaction in MeOH is considerably slower than that in water.²⁴ For the reaction of **1**, however, the change of solvent from water to MeOH has no effect on the rate, which supports the rate-determining fragmentation from **3**.

Thus, it may be concluded that the decomposition proceeds via the rate-determining fragmentation of **3** according to Scheme III. The 15-fold enhancement of rate by one phenyl group is probably due to its electron attraction, increasing the equilibrium concentration of **3**.²⁵ A similar order, i.e., PhCN > MeCN, is also reported for the formation of peroxy-carbimide acid RC(OOH)=NH by the base-catalyzed addition of H₂O₂ to RC≡N.²⁸

It is well known that excited ketone is formed in high quantum yield ($\Phi > 0.1$) by the thermolysis of isolable dioxetanes.^{11,12} Much lower yields of chemiluminescence ($\Phi = 10^{-4}$ - 10^{-6}) are observed for the base-catalyzed decompositions of α -hydroperoxy ketones⁶ and esters,⁷ which are explained by the fact that the predominant reaction is via an acyclic pathway. In contrast, the present reaction of **1** proceeds solely via the cyclic mechanism (Scheme III), but the chemiluminescence yield is very low ($\Phi = 10^{-8}$ - 10^{-6}). This contrast is probably due to the fact that the intermolecular additions of RO⁻ to ketones and esters are much easier than the addition to nitriles. It may be essential that a lower yield is always observed in the decomposition of dioxetanes with α anion such as **3**. Recently, a low yield ($\Phi \sim 10^{-2}$) of chemiluminescence

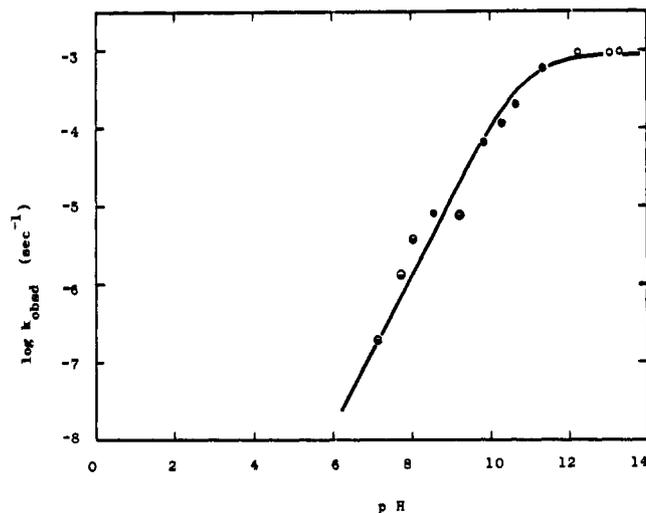


Figure 1. The pH-rate profile for base-catalyzed decomposition of **1a** in water at 25 °C (see Table IIA for data): ○, NaOH; ●, carbonate buffer; ●, phosphate buffer. The solid line is calculated assuming $\text{p}K_{\text{a}} = 10.9$ and $k_1 = 0.87 \times 10^{-3} \text{ s}^{-1}$, where k_1 is the rate constant for the disappearance of **1A**, i.e., $v = k_1[\mathbf{1A}]$.

was reported with a neutral dioxetane.²⁹ These facts suggest that a dioxetane mechanism cannot be ruled out solely by the absence of chemiluminescence.

Experimental Section

Melting points were corrected but boiling points were uncorrected. IR and NMR spectra were recorded on a Perkin-Elmer 337 spectrophotometer and a Hitachi R-24B NMR spectrometer using Me₄Si as an internal standard. The GLC analysis was performed with a Yanagimoto 550-F gas chromatograph using two columns (1 m): PEG 20M, 2% on Chamelite CK; Silicone SE-30, 10% on Chromosorb.

Materials. α -Methylbenzyl cyanide and α -phenylbutyronitrile were synthesized by *t*-BuOK-catalyzed alkylation of benzyl cyanide. Thus, *t*-BuOK (19.5 g, 0.105 mmol) was added in small portions under N₂ to a mixture of benzyl cyanide (11.7 g, 0.10 mmol) and methyl iodide (14.9 g, 0.105 mmol) in DMF (40 mL)-*t*-BuOH (10 mL) and stirred for 1 h at room temperature. The reaction mixture was poured into 5% aqueous AcOH; extraction with benzene and rectification afforded α -methylbenzyl cyanide (9.7 g, 74%), bp 102-104 °C (10 mm) (lit.³⁰ 107-110 °C (11 mm)). α -Phenylbutyronitrile was prepared in 55% yield similarly from ethyl bromide, bp 107-108 °C (9 mm) (lit.³¹ 105-110 °C (8 mm)).

1,2-Diphenylpropionitrile was prepared in 35% yield by heating a mixture of PhCH₂Cl, PhCH₂CN, and powdered NaOH (1:1:1.5 molar ratio) at 100 °C for 15 h, bp 182-184 °C (7 mm) and mp 55 °C (lit.³² mp 56 °C). Commercial diphenylacetone and isobutyronitrile were used; they showed a single peak in GLC analysis.

α -Hydroperoxy Nitriles (1). Powdered *t*-BuOK (1.15 g, 10 mmol) was added at -60 °C in three portions to the starting nitrile (5 mmol) in 1,2-dimethoxyethane (40 mL) into which oxygen was bubbled gently. After 10 min of bubbling, the reaction mixture was poured into

dilute phosphoric acid and extracted with ether, which was washed with aqueous carbonate buffer ($\text{NaHCO}_3\text{-Na}_2\text{CO}_3$, 1:1) and then with water. Iodometry indicates 40–80% yields of peroxide formation. The crude peroxide **1** was purified by passing through a Florisil column using *n*-hexane, *n*-hexane- CH_2Cl_2 (3:1), and then CH_2Cl_2 . Elution of the peroxide was easily monitored by iodometry. Evaporation of CH_2Cl_2 under slightly reduced pressure afforded α -hydroperoxy nitrile in 20–50% yields, some of which (**1b–d**) could be crystallized by standing in a refrigerator for 2–10 days and washing with *n*-hexane. Melting points are listed in Table IV.

Attempted preparations of **1** by the reaction at -20°C or in dimethylformamide-monomer at -60°C were unsuccessful (titrated yield <2%). The washing with aqueous carbonate buffer was effective in decomposing contaminated cyanohydrin.

The purity of peroxide **1** was determined iodometrically in $\text{MeOH-AcOH-H}_2\text{O}$ (2:1:1).⁶ The structure of $\text{R}_1\text{R}_2\text{C}(\text{OOH})\text{CN}$ was established by IR and NMR spectra (Table IV), and by the KI reduction to cyanohydrins.

Rates and Products. The rate of base-catalyzed decomposition of **1** was followed up to 80% conversion by iodometry⁶ and found to be first order in **1**. The reproducibility of the k_{obsd} value was adequate (within $\pm 5\%$) in the presence of EDTA, although its absence did not affect the value in most cases.

Organic products were determined by GLC analysis using propiophenone or biphenyl as an internal standard. Cyanide ion could not be detected even by benzidine-cupric acetate test.⁹ Quantitative formation of cyanate ion was reported for the reaction of **1a**.⁴

Chemiluminescence. Chemiluminescence was monitored by a Hitachi MPF-2A fluorescence spectrophotometer using a 3-mL solution in a 4-mL quartz cell. The initial intensity at time zero was determined from the plot of *I* vs. time. The quantum yields were calculated according to the reported method^{7,33} using the equation in footnote *d*, Table III. The incident light from a Xe arc was determined by ferrioxalate actinometry.³⁴

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A Model for the Transition State of the Reduction of Aliphatic Ketones by Sodium Borohydride

Jean-Claude Perlberger and Paul Müller*

Contribution from the Département de Chimie Organique, Université de Genève, 1211 Genève, Switzerland. Received August 16, 1976

Abstract: A simple model for the transition state of the ketone reduction with sodium borohydride is proposed. The strain energy of this model is calculated by means of a molecular mechanics program. It allows us to rationalize the distribution of epimeric alcohols formed from a given ketone with an average uncertainty of $\pm 10\%$ and the reduction rates over a rate range of 10^8 and an average error by a factor of 10.

The interpretation of the reduction rates of aliphatic ketones with complexed hydrides such as sodium borohydride or lithium aluminum hydride represents an old, but still unresolved, problem for mechanistically inclined chemists. The understanding of the reaction is also of interest from the syn-

thetic viewpoint, as it should allow predictions concerning the regio- and stereospecificity of the ketone reduction.

The reaction of sodium borohydride with ketones in 2-propanol solution exhibits simple second-order kinetics; it is first order both in hydride and ketone.¹ The rate-determining step