data were then refit by unweighted least squares to the equation $y = a_1x$, and the calculated value of $a_1$ was taken as the second-order rate constant $k_1$.

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# Rearrangements of Nitrones to *O*-Alkyl Oximes via Geometrically Isomerizing Iminoxy Radicals[1]

**Thomas S. Dobashi, David R. Parker, and Edward J. Grubbs***

*Contribution from the Department of Chemistry, San Diego State University, San Diego, California 92182.* *Received November 29, 1976*

**Abstract:** The isomeric *N*-benzhydryl-α-phenyl-α-*p*-tolylnitrones ((*E*)-**1** and (*Z*)-**1**) have been prepared and separated. The stereochemical courses of their thermal rearrangements to the *O*-benzhydryl *p*-methylbenzophenone oximes ((*E*)-**4** and (*Z*)-**4**) have been determined in *tert*-butyl alcohol. Initial rates of the N to O rearrangements have been measured in the same solvent. Using these data, the rates of interconversion of the intermediate *E* and *Z* iminoxy radicals have been estimated. Rates and activation parameters for the geometric isomerization of (*E*)- and (*Z*)-sodium *p*-methylbenzophenone oximate in methanol are reported. These data are discussed in terms of mechanisms for the N to O rearrangement and syn-anti isomerizations.

*N*-Benzhydryl-α,α-diarylnitrones are known to undergo thermal isomerization to corresponding *O*-benzhydryl oximes (*O*-ethers).[2,3] However, the decomposition of these nitrones is more complicated than earlier envisioned. The available evidence[4–7] now indicates that the decomposition involves the formation of iminoxy and benzhydryl radicals. Among several options available to these geminately formed radicals is the recombination at oxygen to form the *O*-ethers both intra- and intermolecularly.[6]

In the present study, the geometric courses of the N to O rearrangements of the syn and anti nitrones, (*Z*)-**1** and (*E*)-**1**, have been determined. The results of this study lead to an estimate of the rates of geometric isomerization of the intermediate iminoxy radicals (*Z*)-**2** and (*E*)-**2**. A striking contrast is observed between these rate constants and those for the geometric isomerizations of the corresponding oxime anions (*Z*)-**5** and (*E*)-**5**. These data are discussed in terms of possible mechanisms of these isomerizations.

## Results

**Syntheses of the Nitrones and *O*-Benzhydryl Oximes and Geometric Assignments.** A mixture of the nitrones (*Z*)-**1** and (*E*)-**1** was prepared by the reaction of *p*-tolylphenylketimine with *N*-benzhydrylhydroxylamine by a procedure similar to that described previously.[3] The isomers were resolved by fractional crystallization. Geometric assignments were made by a $^1H$ NMR method based upon the multiplicity characteristics of the ortho protons of the α-aryl ring cis to the oxygen atom.[8,9] Thus (*Z*)-**1** exhibits a low-field two-proton doublet at δ 7.99 which can be attributed to the ortho protons on an α-aryl ring which is (a) substituted in the para position and (b) cis to the oxygen atom. The doublet is presumably half of the AA′BB′ signal involving coupling of the ortho protons to the meta protons which are obscured in the remaining complex aromatic multiplet at higher field. By contrast the two-proton absorption for (*E*)-**1** in the region δ 8.14–7.43 is a complex multiplet.

The two *O*-benzhydryl oximes, (*Z*)-**4** and (*E*)-**4**, were prepared by the alkylations of the geometrically pure oxime anions employing benzhydryl bromide in acetone. The geometric assignments were based upon the assumption that geometric retention of configuration was maintained during the alkylations.[10] This is also consistent with the observed configurational stability of these oxime anions described below. Further support for these assignments comes from the composition of the *O*-ethers obtained from thermolyses (interrupted at early stages of the decompositions) of isomerically pure[12] nitrones.

**Thermal Decompositions of Nitrones. *O*-Ether Product Composition as a Function of Percent Nitrone Decomposition.**

Table I. Geometric Compositions of $N$-Benzhydryl Nitrones ($Z$)-**1** and ($E$)-**1** and $O$-Benzhydryl Oximes ($Z$)-**4** and ($E$)-**4** Recovered from Partial Decompositions of the Isomeric $N$-Benzhydryl-$\alpha$-($p$-tolyl)-$\alpha$-phenylnitrones at 144 °C

| | | | Geometric composition | |
|---|---|---|---|---|
| Nitrone | Solvent | % dec of nitrone[a] | Nitrones ($E$)-**1**/($Z$)-**1** | $O$-Benzhydryl oximes ($E$)-**4**/($Z$)-**4** |
| ($E$)-**1** | DEC[b] | 7 | 85/15 | 62/38 |
| ($E$)-**1** | DEC | 22 | 69/31 | 53/47 |
| ($E$)-**1** | DEC | 40 | 52/48 | 47/53 |
| ($Z$)-**1** | DEC | 10 | 19/81 | 32/68 |
| ($Z$)-**1** | DEC | 30 | 35/65 | 38/62 |
| ($Z$)-**1** | DEC | 48 | 45/55 | 39/61 |
| ($E$)-**1** | $t$-BuOH | 4 | 91/9 | |
| ($E$)-**1** | $t$-BuOH | 6 | 90/10 | 60/40 |
| ($E$)-**1** | $t$-BuOH | 8 | 83/17 | 62/38 |
| ($E$)-**1** | $t$-BuOH | 8 | 82/18 | |
| ($E$)-**1** | $t$-BuOH | 25 | | 54/46 |
| ($E$)-**1** | $t$-BuOH | 25 | 66/34 | 56/44 |
| ($E$)-**1** | $t$-BuOH | 49 | 49/51 | 50/50 |
| ($E$)-**1** | $t$-BuOH | 49 | 53/47[c] | 52/48[c] |
| ($E$)-**1** | $t$-BuOH | 69 | 49/51 | 49/51 |
| ($Z$)-**1** | $t$-BuOH | 5 | 10/90 | 30/70 |
| ($Z$)-**1** | $t$-BuOH | 10 | 17/83 | 31/69 |
| ($Z$)-**1** | $t$-BuOH | 31 | 36/64 | 37/63 |
| ($Z$)-**1** | $t$-BuOH | 49 | 48/52 | 39/61 |
| ($Z$)-**1** | $t$-BuOH | 69 | 49/51 | 42/58 |
| ($Z$)-**1** | $t$-BuOH | 75 | 49/51 | 43/57 |

[a] Calculated from first-order rate constants for the $N$-benzhydryl nitrones (see Table II). [b] Diethyl carbitol. [c] Elemental analyses were obtained for these samples. Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14. Found for nitrone: C, 85.95; H, 6.02. Found for $O$-benzhydryl oxime: C, 85.91; H, 6.10.

Table II. First-Order Rate Constants for the Thermal N to O Rearrangement of Nitrones ($E$)-**1** and ($Z$)-**1** in *tert*-Butyl Alcohol[a] at 144 °C

| Nitrone | $k_i{}^b \times 10^5$, s$^{-1}$ |
|---|---|
| ($E$)-**1** | 1.12 ± 0.12 |
| ($E$)-**1** | 0.92 ± 0.11 |
| ($Z$)-**1** | 1.39 ± 0.05 |
| ($Z$)-**1** | 1.43 ± 0.08 |

[a] Initial concentrations of nitrones ~3.6 × 10$^{-3}$ M. [b] First-order rate constants, $k_{\text{initial}}$, determined from 0–10% reaction.

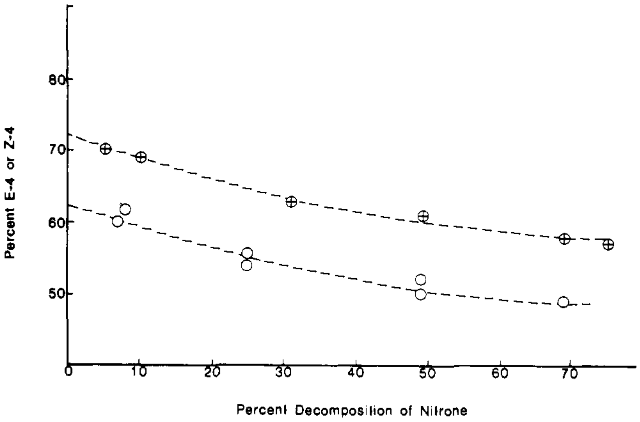


Figure 1. Plot of composition of $O$-benzhydryl-$p$-methylbenzophenone oximes (○ for % ($E$)-**4** from nitrone ($E$)-**1** and ⊕ for % ($Z$)-**4** from nitrone ($Z$)-**1**) formed from nitrone decompositions in *tert*-butyl alcohol at 144 °C.

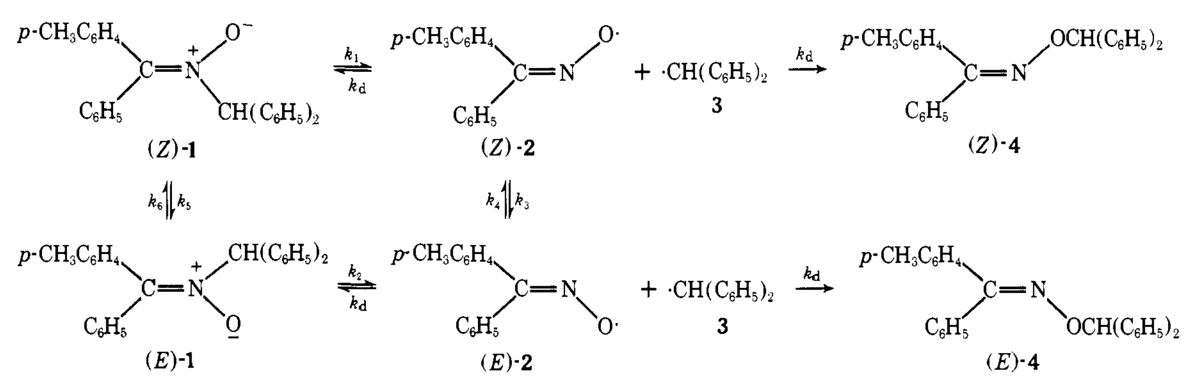
Geometrically pure nitrones were subjected to thermal decomposition in degassed *tert*-butyl alcohol or bis(2-ethoxyethyl) ether (diethyl carbitol). Because of overlapping chemical shifts for the nitrones and $O$-ethers, direct NMR analyses of product mixtures were not possible. The nitrones and $O$-ethers were thus separated chromatographically and the geometric composition of each determined by its $^1$H NMR spectrum. The results are shown in Table I. The $O$-ethers ($Z$)-**4** and ($E$)-**4** were shown to be stable toward decomposition and configurational isomerization under the conditions leading to greater than 99% decompositions of the nitrones.

Figure 1 shows a plot of the geometric compositions of $O$-ethers (extrapolated to "zero percent decomposition" of nitrone ($Z$)-**1** or ($E$)-**1**) as a function of extent reaction of nitrone in *tert*-butyl alcohol.

**Kinetics of the Thermal Decompositions of (*E*)-1 and (*Z*)-1 in *tert*-Butyl Alcohol at 144 °C.** The rates of disappearance of nitrone were determined spectrophotometrically (UV) making use of their intense absorption near 311 nm. Numerous points were obtained during the first 10% of the decomposition so that "initial" rate constants could be determined. It was necessary to determine rate constants during early stages of the decompositions because, although the two isomeric nitrones decompose at measurably different rates when geometrically pure, they gradually approach an equilibrium mixture (presumably via a competitive rotational process and recombination at nitrogen of equilibrating iminoxy radicals). These "initial" first-order rate constants are listed in Table II.

**Kinetics of the Thermal Geometric Isomerizations of (*Z*)-Sodium *p*-Methylbenzophenone Oximate.** The isomerization rates were conveniently determined by following the changes in intensities of the two methyl proton singlets, the chemical shifts for which differ by approximately 0.07 ppm. Although high-purity solvents were used and careful deoxygenations of solutions were performed, the rate constants (shown in Table III) in some cases have sizable probable errors along with moderate precision. This accounts for the uncertainty in $\Delta S^{\ddagger}$. The activation parameters obtained from the average of the rate constants at each temperature in Table III are $E_a = 26 \pm 2$ kcal/mol, $\Delta S^{\ddagger} = -20 \pm 7$ eu.

Scheme I



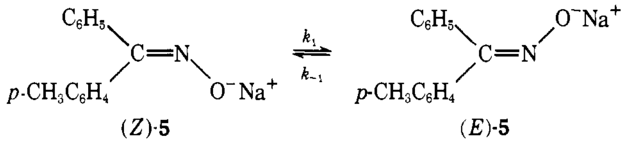
## Discussion

The principal reaction steps occurring during the thermolyses of the nitrones (*Z*)-**1** and (*E*)-**1** in *tert*-butyl alcohol are shown in Scheme I. Evidence for the intermediacy of the benzhydryl and iminoxy radicals from nitrone decompositions in *tert*-butyl alcohol is derived from (a) the stereochemical course of this rearrangement (discussed below), and (b) crossover studies employing *N*-benzhydryl-$\alpha,\alpha$-diphenylnitrone (**6**) and its para-tetradeuterated analogue (**6**-$d_4$) which demonstrate extensive intermolecularity in the N to O rearrangement,[13] and the similarity in rates and activation parameters for the decomposition of *N*-diarylmethyl-$\alpha,\alpha$-diarylnitrones in dimethylacetamide, *tert*-butyl alcohol, and diethyl carbitol.[4,13] In the latter solvent radicals have been detected by electron spin resonance.[5] Caged and free radicals are not distinguished in Scheme I, but possible effects of caged processes are discussed later.

In several previous studies, equilibrium mixtures of geometrically isomeric iminoxy radicals have been observed following the oxidation of isomerically pure oximes.[14] The data in Tables I and II allow one to estimate the rates of geometric isomerization of iminoxy radicals (*Z*)-**2** and (*E*)-**2** in *tert*-butyl alcohol. The isomerization of nitrones (*Z*)-**1** and (*E*)-**1** proved to be competitive[15] with the rates for the N to O rearrangements as can be seen from Table I. Thus in order to determine the geometric compositions of *O*-ethers (*Z*)-**4** and (*E*)-**4** formed from an isomerically pure nitrone it was necessary to extrapolate these compositions to "zero percent decomposition" of the given nitrone. This is shown in Figure 1. These extrapolations lead to the following results. Under the conditions of these studies (144 °C, *tert*-butyl alcohol solvent, initial nitrone concentrations $10^{-2}$–$10^{-3}$ M) pure (*Z*)-**1** produces a mixture of *O*-ethers in a ratio (*Z*)-**4**/(*E*)-**4** of 72/28. The corresponding ratio (*E*)-**4**/(*Z*)-**4** formed from pure (*E*)-**1** is approximately 62/38.[16] Kinetic data for the decompositions of the two nitrones in the same solvent were also analyzed at early stages of the N to O rearrangements prior to substantial geometric equilibration of (*Z*)-**1** and (*E*)-**1**.[17] Thus for (*Z*)-**1**, $k_{\text{obsd}}$ is $1.4 \times 10^{-5}\ \text{s}^{-1}$; for (*E*)-**1** $k_{\text{obsd}}$ is $1.0 \times 10^{-5}\ \text{s}^{-1}$ at 144 °C.

Two observations regarding the stereochemical results are particularly interesting. First, at very early stages of the rearrangements (as measured by nitrone disappearance) when the starting nitrone has undergone little configurational isomerization, the *O*-ethers are formed with extensive configurational isomerization. This is inconsistent with predictions based upon a concerted mechanism[2] and supports the proposal that the products are formed largely from intermediates (iminoxy radicals) that do not maintain their geometric configuration. The second noteworthy point is that *O*-ether compositions indicate that the products are not being formed by the reaction of benzhydryl radicals with iminoxy radicals which have achieved and are maintaining a state of geometric ($k_3/k_4$) equilibrium.

Table III. Kinetic Data for the Thermal Isomerization[a,b] of (*Z*)-Sodium *p*-Methylbenzophenone Oximate in Methanol[c]



| Temp, °C | $k_1 \times 10^5$ |
|---|---|
| 135 | $1.27 \pm 0.11$ |
| | $1.33 \pm 0.48$ |
| 144 | $3.25 \pm 0.25$ |
| | $3.05 \pm 0.22$ |
| | $3.24 \pm 0.18$ |
| | $3.07 \pm 0.27$ |
| 160 | $8.61 \pm 0.60$ |
| | $8.35 \pm 0.90$ |

[a] Data are for $k_1$ in approach to equilibrium. [b] The value of *K* determined by separate approach from both isomer is 0.65. [c] The oximate concentrations were approximately 0.09 M.

With reference to Scheme I, the stereochemical and rate data (Tables I and II) in *tert*-butyl alcohol can be used to estimate the rate constants ($k_3$ and $k_4$) for iminoxy radical geometric isomerization. In doing this we assume that both types of processes involving radical–radical combination (namely, benzhydryl radical recombination at nitrogen or oxygen) are diffusion controlled. The value of $k_d$ in this analysis is assumed to be $10^9$. The effect of the uncertainty of the exact magnitude of $k_d$ upon the derived values of $k_3$ and $k_4$ is discussed later. In a related study[13] crossover experiments employing **6** and **6**-$d_4$ decomposing in *tert*-butyl alcohol have shown that the rate constants (at least for intermolecular reaction) for benzhydryl radical recombination with diphenyliminoxy radicals at oxygen and nitrogen are nearly equal.[18] Using Scheme I, the "steady state" concentrations of iminoxy radicals (*Z*)-**2** and (*E*)-**2** and benzhydryl radicals **3** can be computed at very early stages of the N to O rearrangement. Thus, the rate of disappearance of nitrone (*E*)-**1** measured spectrophotometrically is equal to the rate of product formation, i.e.

$$k_{\text{obsd}}[(E)\text{-}\mathbf{1}] = \{[(E)\text{-}\mathbf{2}] + [(Z)\text{-}\mathbf{2}]\}[\mathbf{3}]k_d$$

We have also shown that *O*-benzhydryloxime formation is nearly quantitative in *tert*-butyl alcohol.[19] Therefore

$$[(E)\text{-}\mathbf{2}] + [(Z)\text{-}\mathbf{2}] = [\mathbf{3}]$$

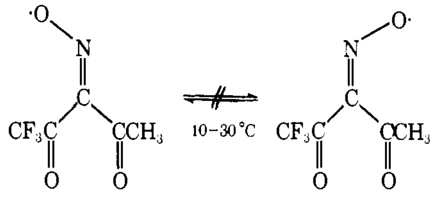
The values of $k_{\text{obsd}}$ ($\sim 1.00 \times 10^{-5}\ \text{s}^{-1}$) and initial [(*E*)-**1**], namely, $3.6 \times 10^{-3}$ M, are known. This leads to a value of $[\mathbf{3}] = [(E)\text{-}\mathbf{2}] + [(Z)\text{-}\mathbf{2}] = 6.02 \times 10^{-9}$ M. Now using the stereochemical data for the decomposition of pure (*E*)-**1**, the ratio [(*E*)-**4**/(*Z*)-**4**] of products formed initially (which from Figure

1 is 1.6) equals the ratio of initial "steady state" concentrations of the iminoxy radicals, $[(E)\text{-}\mathbf{2}/(Z)\text{-}\mathbf{2}]$. Thus, $[(E)\text{-}\mathbf{2}]_{\text{init}} = 3.7 \times 10^{-9}$ M and $[(Z)\text{-}\mathbf{2}]_{\text{init}} = 2.3 \times 10^{-9}$ M. From the steady state approximation for $[(E)\text{-}\mathbf{2}]$ one obtains

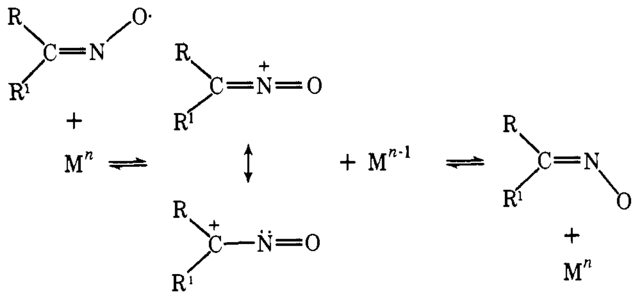
$$k_2[(E)\text{-}\mathbf{1}] + k_3[(Z)\text{-}\mathbf{2}] = 2k_d[\mathbf{3}][(E)\text{-}\mathbf{2}] + k_4[(E)\text{-}\mathbf{2}] \tag{1}$$

And since $k_2 = 2k_{\text{obsd}}$ in this scheme,[20] all quantities in eq 1 are known except $k_3$ and $k_4$. The ground states of nitrones (*Z*)-**1** and (*E*)-**1** are identical within experimental error.[21] Thus a value of $k_3/k_4 = 0.7$ can be deduced from the initial first-order rate constants for decomposition of (*Z*)-**1** and for (*E*)-**1** ($1.4 \times 10^{-5}$ and $1.0 \times 10^{-5}$ s$^{-1}$, respectively). If this ratio is now combined with the other known quantities in eq 1, the rate constants $k_3 = 9$ s$^{-1}$ and $k_4 = 13$ s$^{-1}$ are obtained. A value of $10^{10}$ may be a better estimate for the value of the diffusion-controlled rate constant under these conditions. If this is the case, magnitudes of these rate constants would be increased by a factor of $(10)^{1/2}$, i.e., $k_3 = 28$ s$^{-1}$ and $k_4 = 41$ s$^{-1}$. These values may still be somewhat low because of the possibility of cage recombination occurring with higher retention of geometric configuration.[22]

Relatively few data bearing on the rates of syn-anti isomerization are available in the literature to compare with our values of $k_3$ and $k_4$. Norman and Gilbert (private communication) have placed a *lower limit* of about 30 s$^{-1}$ for the interconversion of the iminoxy radicals obtained by oxidation of benzil monoximes in a flow system at room temperature. However, even under these conditions, only equilibrium mixtures were observed; thus the rate constants may be considerably higher than this lower limit estimate. If a preexponential Arrhenius factor of $10^{13}$ is assumed for our syn-anti isomerizations (giving an estimated $E_a$ of 22 kcal) $k_2$ and $k_3$ at 25 °C would be approximately $4 \times 10^{-4}$ s$^{-1}$. When compared with Norman and Gilbert's lower limit estimate, our rates appear remarkably slow. Furthermore, Ingold and Brownstein[23] have observed a configurational interchange rate constant for the di-*tert*-butyliminoxy radical of about $6 \times 10^5$ s$^{-1}$ at 14 °C using ESR techniques. To further complicate the picture, Wolodarsky and Wan[24] have reported that the acetyltrifluoroacetyliminoxy radical (**7**) generated as **7a** from trifluoroacetylacetone by $NO_2$ is configurationally stable in chlorocarbon solvents within the temperature range (10-30 °C) studied. There is no apparent reason to anticipate such large differences in rates of *thermal* syn-anti iminoxy radical isomerizations (usually assumed to proceed via a lateral shift). Thus, it would seem prudent to consider mechanisms involving catalysis particularly for the faster rates. One reasonable possibility would appear to be trace metal-ion catalysis. A reversible electron transfer involving a multivalent metal ion could effect geometric isomerizations of iminoxy radicals via an intermediate nitrosodialkyl (or diaryl) cation **8**. Bird and Diaper[25] have studied the stoichiometry and calorimetry of ceric(IV) oxidations of several ketoximes in aqueous solutions containing an alcohol or acetonitrile. They propose that the initially formed iminoxy radicals undergo a further one-electron oxidation giving intermediates **8** which are trapped by water.[26] The interesting question is whether the one-electron oxidation of iminoxy radicals is reversible. The reported[24] configurational stability of **7a** may reflect the absence of trace metal ions (note that metals are not used in the generation of the radical). Or this iminoxy radical may simply resist oxidation because of the instability of the corresponding cation which would have $CF_3CO$ and $CH_3CO$ groups attached to the central electron-deficient carbon.[28] Clearly these proposals suggest several lines of further investigation which may help establish the basis for these divergent rate data for syn-anti isomerizations of iminoxy radicals.



**7a** **7b**



**8**

Our experience with the stereospecific phenylation of (*Z*)-sodium 4-methylbenzophenone oximate[9] suggested that a comparison of its $Z \rightleftharpoons E$ interconversion with that of the corresponding iminoxy radicals would be of interest. Surprisingly, almost no kinetic data for oxime anion geometric isomerizations have been previously published.[29] Referring to Table III, it is seen that under reasonably comparable conditions, the iminoxy radical geometric interconversion rate is approximately $10^6$ faster than that of the corresponding oximates. However, speculation concerning the origin of this rate difference must be deferred until there is greater certainty that both systems represent uncatalyzed, thermal isomerizations. It is interesting to note that the value $k_3/k_4$ (0.7) estimated indirectly for the iminoxy radical interconversions is equal, within experimental error, to the equilibrium constant (0.65) directly obtained for the isomerizations of the corresponding oximates.

The oxime anions and iminoxy radicals probably isomerize thermally via a lateral shift (as opposed to rotation). A calculated (CNDO/2) barrier for a "lateral shift" of acetone oxime anion (28 kcal/mol)[32] is close to our measured value of 26 kcal/mol for the isomerization of (*Z*)-**5** to (*E*)-**5**. Although the agreement is certainly fortuitous, the much higher value calculated for a rotational transition state renders this pathway very unlikely. Interestingly, a recent CNDO/2 calculation[33] of the energy barrier for "isomerization" of the dimethyliminoxy radicals via a linear (C-N-O) transition state (27 kcal/mol) is almost identical with that for the oxime anion. Again a rotational barrier is calculated to be much higher.

## Experimental Section[34]

**(*Z*)-*p*-Tolyl phenyl ketoxime** was separated from a mixture containing its geometric isomer by crystallization from ethanol following previously described procedures.[35] It was obtained as colorless needles: mp 153-155 °C (lit.[36] mp 155-157 °C); NMR (pyridine) $\delta$ 2.30, *p*-$CH_3$; UV ($C_2H_5OH$) $\lambda_{\max}$ ($\epsilon$) 235.0 nm (16 500) (lit.[36] 235 nm (16 000); IR (KBr) 950 (N-O), 818 (para-disubstituted aromatic C-H bend), and 693 cm$^{-1}$ (monosubstituted aromatic C-H bend).

**(*E*)-*p*-Tolyl phenyl ketoxime** was also obtained as above as colorless needles: mp 136.5-139 °C (lit.[36] mp 136-137.5 °C); NMR (pyridine) $\delta$ 2.22, *p*-$CH_3$; UV ($C_2H_5OH$) $\lambda_{\max}$ ($\epsilon$) 234.0 nm (14 970) and 256.0 (12 620) (lit.[36] 234 nm (15 400) and 256 (13 000)); IR (KBr) 984 (N-O), 822 (para-disubstituted aromatic C-H bend), and 695 cm$^{-1}$ (monosubstituted aromatic C-H bend).

**(*Z*)-*O*-Benzhydryl-*p*-methylbenzophenone oxime** ((*Z*)-**4**) was prepared by a method previously described by Smith and Robertson[37] for the syntheses of some *O*-benzylbenzophenone oximes. From 1.09 g (5.15 mmol) of the *Z* oxime and 1.35 g (5.45 mmol) of benzhydryl bromide was obtained 0.870 g (45%) of (*Z*)-**4** as a white powder (from ethanol): mp 139-140.5 °C; NMR ($CDCl_3$) $\delta$ 7.48-6.94 (m, 19, aromatic), 6.37 (s, 1, benzhydryl CH), and 2.38 (s, 3, *p*-$CH_3$); UV ($C_2H_5OH$) $\lambda_{\max}$ ($\epsilon$) 263 nm (14 390).

Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.83; H, 6.08; N, 3.88.

**(*E*)-*O*-Benzhydryl-*p*-methylbenzophenone oxime ((*E*)-4)** was similarly prepared (51% yield) by alkylation of the isomeric oxime. This isomeric *O*-benzhydryl derivative was obtained as a white powder: mp 84–85 °C; NMR ($CDCl_3$) $\delta$ 7.45–6.89 (m, 19, aromatic), 6.37 (s, 1, benzhydryl CH), and 2.29 (s, 3, *p*-$CH_3$); UV ($C_2H_5OH$) $\lambda_{max}$ ($\epsilon$) 265.5 nm (15 680).

Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.76; H, 6.36, N, 3.52.

**Phenyl-*p*-tolylketimine** was prepared by the addition of *p*-tolunitrile to phenylmagnesium bromide using a procedure described by Pickard and Vaughan[38] for the preparation of other diarylketimines. The ketimine was obtained as a pale yellow liquid in 59% yield: bp 127–131 °C (1.2 mm); NMR ($CCl_4$) $\delta$ 9.45 (s, 1, NH), 7.67–6.80 (m, 9, aromatic), and 2.30 (s, 3, *p*-$CH_3$). This imine was used without further characterization.

**(*E*) and (*Z*)-*N*-Benzhydryl-$\alpha$-(*p*-tolyl)-$\alpha$-phenylnitrone ((*E*)-1 and (*Z*)-1).** The mixture of nitrones was prepared by the reaction of phenyl-*p*-tolylketimine (described above) with *N*-benzhydrylhydroxylamine[39] using a procedure previously reported for the preparation of *N*-benzhydryl-$\alpha,\alpha$-diphenylnitrone.[3] The isomers (initially formed in 66% yield) were separated by fractional crystallizations from methanol. Further purifications of the separated isomers were performed by chromatography on Florisil columns. The nitrones were eluted with benzene/ether (19/1) and recrystallized from methanol.

The *E* isomer was obtained as colorless crystals: mp 151–153 °C; NMR ($CDCl_3$) $\delta$ 8.14–7.43 (m, 2, aromatic), 7.43–6.90 (m, 17, aromatic), 6.43 (s, 1, benzhydryl CH), and 2.41 (s, 3, *p*-$CH_3$); UV (hexane) $\lambda_{max}$ ($\epsilon$) 310.0 nm (16 314); IR (KBr) 1222 $cm^{-1}$ ($N \rightarrow O$); mass spectrum (15 eV) $M^{+\cdot}$ *m/e* 377, P − oxygen 361.

Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.70; H, 6.41; N, 3.61.

The *Z* isomer was isolated as colorless crystals: mp 139–142 °C; NMR ($CDCl_3$) $\delta$ 7.99 (d, 2, aromatic), 7.54–6.93 (m, 17, aromatic), 6.38 (s, 1, benzhydryl CH), and 2.30 (s, 3, *p*-$CH_3$); UV (heptane) $\lambda_{max}$ ($\epsilon$) 312.5 nm (17 970); IR (KBr) 1222 $cm^{-1}$ ($N \rightarrow O$); mass spectrum (15 eV) $M^{+\cdot}$ *m/e* 377, P − oxygen 361.

Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.94; H, 6.11; N, 3.51.

**Thermal N to O Rearrangement Studies of (*Z*)-1 and (*E*)-1. 1. In *tert*-Butyl Alcohol at 144 °C.** A solution of ~30 mg of geometrically pure (*Z*)-1 or (*E*)-1 dissolved in *tert*-butyl alcohol (contained in a Pyrex tube) was degassed (by repetitive freezing, evacuating, admitting $N_2$, thawing, and equilibrating), sealed, and heated in an oil bath. After an appropriate time, the tube was removed from the bath, cooled, and opened. The solution was concentrated to an oil which was chromatographed on a 10 × 300 mm column packed with 60–100 mesh Florisil. Hexane–benzene (4:1) eluted the *O*-benzhydryl oximes as a clear oil. Benzene–ether (9:1) eluted the nitrone as a clear oil which solidified after several hours in vacuo. The NMR spectra (methyl protons) of the *O*-benzhydryl ethers and of the nitrones were used to determine isomer ratios.

**2. In Diethyl Carbitol at 144 °C.** An analogous procedure was used for partial decomposition studies of the nitrones in diethyl carbitol. Since the yield of *O*-benzhydryl oximes was reduced as a result of side reactions, a larger sample of nitrone was used in each decomposition.

Control experiments demonstrated that (a) geometrically pure nitrones and *O*-benzhydryl oximes are configurationally stable on a Florisil column and in $CDCl_3$ (conditions employed for separation and spectral analyses), (b) the *O*-benzhydryl oximes are configurationally stable at 144 °C in either *tert*-butyl alcohol or diethyl carbitol for periods required for >99% decomposition of the nitrones. (The configurational stabilities of these products were determined both alone in a given solvent and in the presence of decomposing *N*-benzhydryl-$\alpha,\alpha$-diphenylnitrone.) (c) The starting nitrone is configurationally stable at 80 °C for 12 h in *tert*-butyl alcohol while 2-azobisisobutyronitrile (AIBN) was decomposed in situ.

**Kinetic Measurements of the Thermal Decompositions of the Isomeric Nitrones (*Z*)-1 and (*E*)-1.** First-order rate constants for the decompositions in thoroughly degassed solutions of nitrone in *tert*-butyl alcohol and in diethyl carbitol were measured at 144.0 °C. The nitrone dissolved in freshly distilled solvent was pipetted into 8 × 180 mm glass tubes. After the solutions were degassed, the tubes were sealed under vacuum. The sealed tubes were placed in the constant temperature bath, removed periodically, quenched in ice water, and opened. Care was taken to exclude light during all manipulations of solutions containing nitrone, since photochemical isomerization of this nitrone to oxaziridine can occur. Aliquots from the quenched tubes were diluted with chloroform and analyzed by ultraviolet spectroscopy. In this way the rates were followed by monitoring the decrease in UV absorbances near 311 nm.

**Kinetic Measurements of the Thermal Geometric Isomerizations of (*Z*)-Sodium *p*-Methyl Benzophenone Oximates ((*Z*)-5).** Isomerically pure oxime samples in absolute methanol were converted to the anions with sodium methoxide. The solutions were degassed, sealed in tubes, and immersed in the constant temperature bath. Tubes were periodically removed and quenched in ice water and the extent of isomerization determined by NMR. Changes in intensities of the two methyl-proton singlets (the chemical shifts for which differ by approximately 0.07 ppm) were used to follow the isomerizations. The first-order rate constants were calculated by a method of least squares according to the expression

$$\ln \frac{A_e}{A_e - A} = \frac{k_1}{A_e} t$$

which is the rate law derived from a reversible first-order reaction. In this expression $A_e$ is the mole fraction of one isomer at equilibrium.

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(10) In each alkylation only one *O*-benzhydryl oxime was detected and isolated. In related alkylations of these oxime anions, where the corresponding geometrically pure *N*-methyl or *N*-benzyl nitrone (with unquestioned configuration) was isolated, the nitrone proved to have the same configuration as the starting oxime.[11] Therefore it is virtually assured that the *O*-alkyl oximes have the same geometry as the oxime precursor.

(11) T. S. Dobashi, M. H. Goodrow, and E. J. Grubbs, *J. Org. Chem.*, **38**, 4440 (1973).

(12) The isomeric purities of both nitrones and *O*-benzhydryl oximes can be readily determined by the intensities of the singlets for the methyl protons. For each isomeric pair the chemical shift difference is approximately 0.1 ppm.

(13) J. A. Villarreal and E. J. Grubbs, unpublished data.

(14) See B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc. B*, **86**, 722 (1966), and references cited therein.

(15) For the corresponding *N*-methyl and *N*-benzyl nitrones the first-order isomerization rate constants in *tert*-butyl alcohol at 144 °C were found to be approximately $3.5 \times 10^{-6}$ and $7.3 \times 10^{-6}$, respectively.[11]

(16) These values are estimated to be accurate to within ±2–3%.

(17) The slight curvature observed for each of these first-order plots is not discernible in the corresponding rate plots for the decomposition of *N*-benzhydryl-$\alpha,\alpha$-diphenylnitrone. For (*E*)-1 and (*Z*)-1 the observed first-order constants obtained from about 35–65% reaction differ from $k_{obsd}$ initial by about 5–10%. In the case of (*E*)-1, $k_{obsd}$ is increasing with time and with (*Z*)-1, $k_{obsd}$ is decreasing.

(18) In diethyl carbitol the ratio for the rate of recombination at O/rate of recombination at N is 1.7.[6]

(19) In diethyl carbitol the *O*-benzhydryl oximes are formed in only 30–40% yield because of competing side reactions which include the dimerization of benzhydryl radicals to form *sym*-tetraphenylethane. Thus the stereochemical data for the rearrangements in DEC (although presented in table for comparison) do not lend themselves to the same analysis possible for experiments in *tert*-butyl alcohol.

(20) Using the steady state approximation, $k_{obsd}$ (init) (determined spectrophotometrically) is related to $k_2$, i.e., $k_{obsd}$ (init) $= k_2k_d/(k_d + k_d)$.

(21) This is based upon the geometric composition of nitrones reisolated at late stages of the decomposition of (*Z*)-1 or (*E*)-1. The same observation was made with regard to the corresponding *N*-methyl and *N*-benzyl nitrones, the equilibrations of which are not complicated by N to O rearrangement or decomposition.[11]

(22) The accuracy of these rate constant estimates is limited primarily by two factors. As indicated, the magnitude of the diffusion-controlled rate constant, $k_d$, may well be as large as $10^{10}$ at these temperatures. (See K. U. Ingold in "Free Radicals", Vol. I, J. K. Kochi, Ed., Wiley, New York, N.Y., 1973, p 39, for a discussion of magnitudes of diffusion-controlled rate constants.) A second major uncertainty arises from the question as to whether caged iminoxy–benzhydryl radical pairs recombine with a higher degree of geometric retention than do the corresponding free radicals. We

have demonstrated that approximately 20% of *O*-benzhydryl benzophenone oxime formed from *N*-benzhydryl-α,α-diphenylnitrone under conditions of the present stereochemical study is produced via a caged process. This information was obtained from crossover experiments using mixtures of deuterated and undeuterated nitrone.[13] The maximum error in $k_3$ and $k_4$ which could result from a highly stereospecific caged process can be estimated. In the limiting case, the caged (or less likely concerted) process could be considered as competing with those in Scheme I and yielding the *O*-benzhydryl oxime with 100% geometric retention. If data used in calculating $k_3$ and $k_4$ are corrected for the contribution of this process to rates and stereochemistry of product formation, the revised $k_3$ and $k_4$ values are larger by a factor of approximately 2.

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(28) The reported[24] isomerization of 7a by trace amounts of ethanol could involve reversible addition of ethanol to the carbon–nitrogen bond.

(29) A previous report[30] indicated that the half-life for the levorotatory sodium salt of cyclohexanone-4-carboxylic acid (oxime primarily un-ionized) was 54 times shorter than that for the same salt in 0.1 N NaOH (oxime largely in the form of its anion). This is one indication that oxime anions may be configurationally more stable than their parent oximes, since the above racemization almost certainly proceeds via isomerization about the carbon–nitrogen double bond. Other qualitative observations bearing on the geometrical stability of oxime anions have been noted.[31]

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(34) Melting points are uncorrected. The NMR spectra were obtained on a Varian Model A-60 spectrometer using tetramethylsilane as internal standard. Infrared spectra were obtained on a Perkin-Elmer 621 grating spectrophotometer. Ultraviolet spectra were measured using a Cary Model 14 recording spectrophotometer. Mass spectra were determined on a Hitachi Perkin-Elmer Model RMU-6E spectrometer. Elemental analyses were performed by C. F. Geiger, Ontario, Calif., and by M. H. W. Laboratories, Garden City, Mich.

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# An Electrochemical Investigation of the Effects of Antiaromaticity and Determination of the Increased Antiaromatic Destabilization of Cyclobutenedione upon Reduction

**Reuben D. Rieke,*[1a] C. Kenneth White, Lee D. Rhyne, Mark S. Gordon, John F. W. McOmie,[1b] and Niegel P. Hacker[1b]**

*Contribution from the Chemistry Department, North Dakota State University, Fargo, North Dakota 58102, William Rand Kenan Laboratories of Chemistry, Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514, and School of Chemistry, University of Bristol, Bristol, BS8 1TS, England.*

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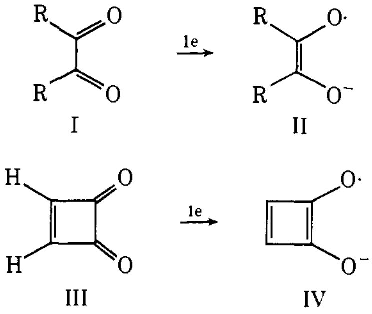
**Abstract:** Electrochemical studies were carried out on a series of cyclic 1,2-diones under nonaqueous conditions. From the reduction potentials and Hückel molecular orbital calculations, the increase in antiaromatic destabilization of cyclobutenedione upon reduction is estimated to be at least 14 kcal/mol. The EPR spectrum of the radical anion of naphtho[*b*]cyclobutadienoquinone is presented. Also, INDO calculations were carried out on several of the diones and the results are consistent with the experimental observations.

Recently there has been considerable interest in small ring compounds possessing four electrons in a π system.[1c,2] Cyclobutadiene is the most studied member of this group of molecules.[1c] There is evidence that the cyclic array of four electrons in a Hückel basis set significantly destabilizes the molecule, and this destabilization is termed antiaromaticity.[1c,2] Owing to the instability of antiaromatic compounds, quantitative estimation of antiaromatic destabilization is difficult and few experimental estimates have been published.[1c] Breslow and co-workers[3] have oxidized hydroquinone anions electrochemically and reported the antiaromatic destabilization of cyclobutadiene to be 15–20 kcal/mol. Recently, Breslow and Sondheimer reported the reduction of some cyclobutenediones.[3]

In this paper we would like to present our attempt to measure the increase in antiaromatic destabilization of cyclobutenedione from the reduction potential of cyclic 1,2-diones (Figure 1). From classical resonance arguments, semidione (II) has increased double bond character between the carbonyl



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