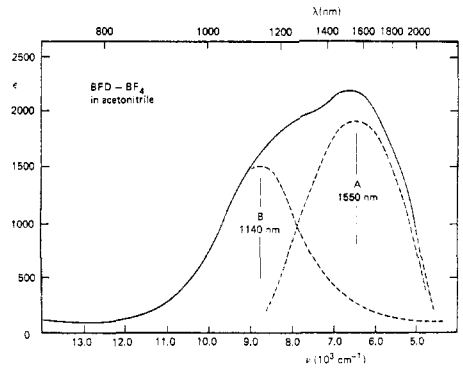

Figure 2. The near-infrared absorption of **6b** in acetonitrile (——) and its decomposition into constituent bands A and B.

columns of cations and anions[19] led us to expect the BFD–TCNQ complex to have two TCNQ units per BFD ("complex" TCNQ salt). A system of this structure should show high conductivity along the main crystal axis, since in addition to the *n*-type conduction within the TCNQ stacks there is the possibility for hole conduction in the columns of BFD cations.[20,21]

BFD was readily oxidized[22] by TCNQ in dichloromethane to give very fine green needles which, after recrystallization from absolute acetonitrile, formed flexible feltlike aggregates. Elemental analysis and electronic spectra proved this product to be the expected bis-TCNQ salt **6c** of the monooxidized BFD. The near-infrared absorption was found to be the same as in **6a** and **6b**. In addition, the absorptions of the complex TCNQ radical anion at 842 and 394 nm were observed to have the intensity found in other TCNQ salts.[23] This shows that even at very low (10^{-4} *M*) concentrations there is no equilibrium between **6c** and neutral BFD and TCNQ. Thus, the BFD–bis-TCNQ complex represents a system with both irreversible (BFD → TCNQ) and reversible (within the cation) electron transfer.

The room temperature bulk conductivity of compressed disks of **6c** was found to be consistently above 10 Ω^{-1} cm^{-1}. This value, which represents the average over the conductivities along the crystal axes and which includes probable losses due to grain boundary effects, gives an indication that an unusually high conductivity along the main crystal axis is to be expected. We have not yet succeeded in obtaining **6c** in single crystals large enough to carry out definitive measurements to determine the magnitude, anisotropy ratios, and the mechanism of its electrical conductivity.

Acknowledgment. We wish to thank Drs. R. L. Greene and B. M. Phipps of this laboratory for the conductivity measurement and Dr. D. O. Cowan for kindly communicating to us some of his results prior to publication.

(19) O. H. LeBlanc, Jr., "Physics and Chemistry of the Organic Solid State," Vol. 3, Interscience, New York, N. Y., p 182ff.

(20) The most recent contribution to the discussion of the conductivity mechanism in TCNQ salts is by A. J. Epstein, S. Etemad, A. F. Garito, and A. J. Heeger, *Phys. Rev. B*, **5**, 952 (1972).

(21) The BFD–bis-TCNQ system could also be viewed as a model compound for organic superconductors according to the theory by W. A. Little (*Phys. Rev. A*, **132**, 1416 (1964)), inasmuch as the TCNQ columns represent the spine of such a system, while the BFD mixed valence cations correspond to the polarizable side chain of this model.

(22) Neither ferrocene nor bisferrocene **4**, $n = 0$, reacted with TCNQ under the same conditions.

(23) Y. Iida, *Bull. Chem. Soc. Jap.*, **42**, 71, 637 (1969).

(24) IBM Postdoctoral Fellow, on leave from the TH Darmstadt, Germany.

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Received September 29, 1972

Synthesis and Structure Determination of a Thermally Labile *anti*-Alkyl Aryl Ketoxime

Sir:

In the course of an investigation of the use of oximes of phenacyl halides as reagents for enzyme modification, it was of interest to compare the relative reactivity of the syn and anti isomers[1] of these compounds. The preparation of *anti*-α-bromoacetophenone oxime was first reported in 1901 by Korten and Scholl[2] from the reaction of α-bromoacetophenone with hydroxylamine hydrochloride in methanol. They isolated two products: *syn*-α-bromoacetophenone oxime (I), mp 97°, and a material, mp 92°, to which they assigned the anti structure, based on the belief current at that time that Beckmann rearrangements occurred by syn migration. Despite the obvious misassignment of the latter structure due to the erroneous interpretation of the Beckmann rearrangement pathway, the Korten and Scholl assignment of the stereochemistry of the 92° melting isomer remained accepted[3] until 1967 when it was proposed[4] that this material was a mixture of α-bromoacetophenone oxime and α-chloroacetophenone oxime (mp 89°) produced by halogen exchange. This proposal was later confirmed by Blumbergs, *et al.*[5] Our own mass spectrometric and nmr measurements show that the crude reaction mixture giving rise to the 92° melting material contains mainly *syn*-α-bromoacetophenone oxime and *syn*-α-chloroacetophenone oxime together with a few per cent of the anti isomers. From this mixture, only the syn isomers were isolated.

Since from the above discussion it is clear that *anti*-α-haloacetophenone oximes had not in fact been prepared previously, the synthesis of *anti*-2-bromoacetophenone oxime (II) was undertaken. The preparation of II and the X-ray determination of its structure are reported in this communication.

The reaction sequence used for the preparation of II is outlined in eq 1. Addition of 5×10^{-2} mol of I in 100 ml of CH_2CN to a solution of 0.5 mol of morpholine in 1.0 l. of H_2O at pH 9.5, followed by $CHCl_3$ extraction and crystallization ($CHCl_3$–petroleum ether), gave 3.4×10^{-2} mol of *anti*-α-morpholinoacetophenone oxime (III): mp 121–122° (lit.[3] mp 116–120°); nmr ($CDCl_3$) δ 7.2–7.7 (5 H, m), 3.5–3.8 (4 H, m), 3.35 (2 H, s), and 2.35–2.65 (4 H, m).[6] III (1.36×10^{-2} mol) was refluxed overnight with 6.8×10^{-2} mol of 2-methoxy-

(1) Throughout this article, syn refers to the isomer having the alkyl group cis to the oxime oxygen; anti refers to the isomer having the akyl group trans to the oxime oxygen.

(2) H. Korten and R. Scholl, *Chem. Ber.*, **34**, 1901 (1901).

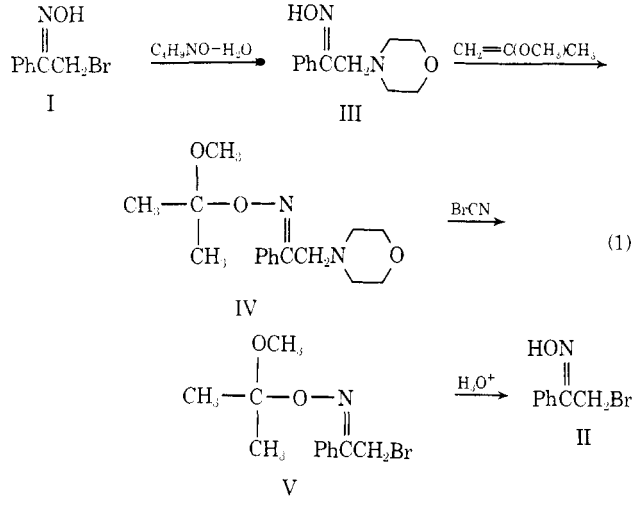
(3) H. P. Fischer and C. A. Grob, *Helv. Chim. Acta*, **45**, 2528 (1962).

(4) M. Masaki, K. Fukui, and M. Ohta, *J. Org. Chem.*, **32**, 3564 (1967).

(5) P. Blumbergs, C. B. Thanawalla, A. B. Ash, C. N. Lieske, and G. M. Steinberg, *ibid.*, **36**, 2023 (1971).

(6) This first step involves an isomerization reaction (*vide infra*).

propene[7] and 7×10^{-4} mol of toluenesulfonic acid·H_2O in 50 ml of CH_2Cl_2. After extraction with K_2CO_3 solution and drying over Na_2SO_4, the solvent was evaporated from the reaction mixture and the residue crystallized from petroleum ether to give 1.03×10^{-2} mol of the *anti*-α-morpholinoacetophenone oxime ketal (IV): mp 62.5–64.0°; nmr ($CDCl_3$) δ 7.3–7.7 (5, m), 3.6–3.8 (4 H, m), 3.4 (2 H, s), 3.2 (3 H, s), 2.4–2.6 (4 H, m), and 1.45 (6 H, s). The protected α-morpholino oxime IV was converted to the protected bromo oxime V *via* the von Braun reaction.[8] After allowing IV (7.8×10^{-3} mol) and cyanogen bromide (7.8×10^{-3} mol) to stand in 12 ml of $CHCl_3$ for 20 min at room temperature, the darkened reaction mixture was filtered and the solvent removed by evaporation. The resulting oil was chromatographed on silica gel (50 g, benzene) to give 1.9×10^{-3} mol of a clear, colorless oil, V: nmr ($CDCl_3$) δ 7.3–7.5 (5 H, m), 4.35 (2 H, s), 3.2 (3 H, s), and 1.45 (6 H, s). The yield in this reaction varied from 25 to 50%. V (1.9×10^{-3} mol) in 10 ml of CH_3CN was added to a mixture of 100 ml of 0.1 *M* HCl and 40 ml of CH_3CN which was stirred at room temperature for 7 min. Extraction with $CHCl_3$, followed by evaporation of the solvent, gave a material which was crystallized twice from $CHCl_3$–petroleum ether to give 1.05×10^{-3} mol of *anti*-α-bromoacetophenone oxime (II): mp 114.0–114.5°;[9] nmr ($CDCl_3$) δ 7.4–7.6 (5 H, m), 4.3 (2 H, s). The nmr absorption due to the methylene protons in the anti isomer II occurs at 0.12 ppm higher field in both $CDCl_3$ and chlorobenzene than the corresponding absorption in the syn species I. The uv spectrum of the anti isomer II in ethanol has λ_{max} 240 nm (log ε 3.91) compared to λ_{max} 254 nm (log ε 3.97) for the syn isomer. Thermal isomerization of the anti isomer II in chlorobenzene at 100° for 1 hr gave an equilibrium mixture of isomers, consisting of about 87% syn and 13% anti species, from which the syn isomer I, identified by a mixture melting point with authentic material, was isolated.



The reaction sequence of eq 1 involves a crucial isomerization step, the conversion of I to III, and the assignment of the stereochemistry of II rests heavily on the accuracy of the identification by Fischer and Grob,[3] using chemical and physical methods, of the geometry

(7) H. P. Crocker and R. H. Hall, *J. Chem. Soc.*, 2052 (1955).
(8) H. A. Hageman, *Org. React.*, 7, 198 (1953).
(9) Satisfactory ir, mass spectral, and analytical data were obtained for II.

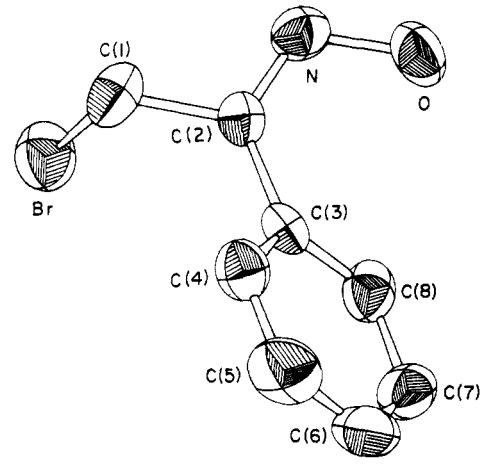


Figure 1. Structure of *anti*-α-bromoacetophenone oxime.

of the oxime function in III. Furthermore, as outlined above, considerable confusion concerning the identification of II existed in the literature prior to the present work. Therefore, to establish on an absolute basis the identity of the material we have synthesized as II, the determination of its structure by X-ray diffraction study was undertaken.

anti-α-Bromoacetophenone oxime (II) crystallized in a tetragonal cell of dimensions $a = b = 12.056 \pm 0.013$ and $c = 12.109 \pm 0.023$ Å; Laue group $4/m$. The experimental density of 1.63 ± 0.03 g/cm³ compared favorably with the calculated density of 1.62 g/cm³, $Z = 8$. From consideration of the distribution of peaks in Patterson space, a space group assignment of $I\bar{4}$ was made.

Data were taken on two axes ($a:h = 0$–3; $c:l = 0$–12) using an automated diffractometer of Weissenberg geometry (Cu Kα radiation). A Fourier synthesis using as a phasing model the position of the bromine atom located from the Patterson map resulted in $R_1 = 0.29$ and peaks corresponding to the ten other nonhydrogen atomic positions. Four cycles of full-matrix least-squares refinement with individual isotropic temperature factors for the 777 independent reflections above background lowered R_1 to 0.091. Two additional cycles of anisotropic refinement produced a final $R_1 = 0.052$. As can be seen from the structure shown in Figure 1, the assignment of anti stereochemistry for II was confirmed. Atomic distances and angles with their associated standard errors are given in Table I and the final atomic positions in Table II.[10]

The syn to anti isomerization process involved in the formation of III from I is typical of the reactions of *syn*-α-haloacetophenone oximes with various nucleophiles in aqueous solution. Such processes have been used in the preparation of several thermally labile *anti*-alkyl aryl ketoximes.[11] In the following communication a mechanistic investigation of the aqueous solvolyses of phenacyl halide oximes is reported.

Acknowledgment. The support of this research by a grant from the Petroleum Research Fund, administered by the American Chemical Society (E. T. K.), a grant

(10) Full details of the crystal-structure determination will be published elsewhere. A table of observed and calculated structure factors is available on request from J. W. M.
(11) J. H. Smith and E. T. Kaiser, unpublished observations.

Table I. Bond Distances and Angles in *anti*-α-Bromoacetophenone Oxime

Bond	Distance, Å	Esd	Angle	Deg	Esd
Br–C(1)	1.968	0.008	Br–C(1)–C(2)	109.0	0.5
C(1)–C(2)	1.509	0.010	C(1)–C(2)–C(3)	120.3	0.7
C(2)–C(3)	1.474	0.011	C(1)–C(2)–N	112.5	0.7
C(2)–N	1.291	0.010	N–C(2)–C(3)	127.2	0.6
N–O	1.409	0.008	C(2)–N–O	113.5	0.7
C(3)–C(4)	1.404	0.010	C(2)–C(3)–C(4)	119.3	0.7
C(4)–C(5)	1.366	0.015	C(2)–C(3)–C(8)	122.1	0.6
C(5)–C(6)	1.358	0.015	C(4)–C(3)–C(8)	118.6	0.7
C(6)–C(7)	1.389	0.015	C(3)–C(4)–C(5)	120.5	0.8
C(7)–C(8)	1.385	0.014	C(4)–C(5)–C(6)	121.0	0.9
C(8)–C(3)	1.402	0.011	C(5)–C(6)–C(7)	120.0	0.9
			C(6)–C(7)–C(8)	120.3	0.9
			C(3)–C(8)–C(7)	119.6	0.8

Table II. Final Atomic Positions for *anti*-α-Bromoacetophenone Oxime

Atom	*x/a*	*y/a*	*z/c*
Br	0.4587 (1)	1.2989 (0)	0.5470 (1)
C(2)	0.3219 (7)	1.2315 (6)	0.6050 (8)
C(3)	0.3228 (6)	1.1089 (6)	0.5798 (7)
N	0.3599 (5)	1.0505 (5)	0.6611 (6)
O	0.3604 (6)	0.9356 (5)	0.6400 (6)
C(6)	0.2800 (6)	1.0677 (5)	0.4734 (6)
C(7)	0.1792 (6)	1.1092 (6)	0.4327 (9)
C(8)	0.1365 (8)	1.0707 (9)	0.3355 (10)
C(9)	0.1907 (10)	0.9922 (8)	0.2757 (8)
C(10)	0.2919 (9)	0.9511 (8)	0.3123 (8)
C(11)	0.3358 (7)	0.9864 (7)	0.4120 (8)

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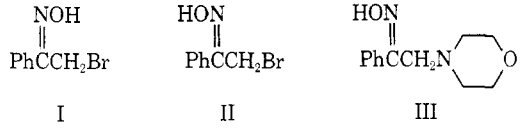
Kinetics and Stereochemistry of Nucleophilic Reactions of Phenacyl Halide Oximes

Sir:

In the preceding communication[1] the synthesis of *anti*-α-bromoacetophenone oxime[2] (II) and the determination of its structure by an X-ray diffraction study were reported. The first step in the reaction sequence leading to II is the conversion of *syn*-α-bromoacetophenone oxime (I) *via* solvolysis in aqueous morpholine buffer to *anti*-α-morpholinoacetophenone oxime (III), a reaction involving the isomerization of a starting material having a thermally favored geometry to a product with a thermally unfavored geometry. While several reports have appeared in the literature[3-7] concerning the reactions of α-halooximes with nucleophiles, the stereochemical consequences, with respect to the oxime function, of these reactions have not been analyzed. In the present communication, we report a kinetic and stereochemical investigation of the mechanism of the solvolysis of α-haloacetophenone oximes in aqueous media.



I II III

At pH values significantly below the pK_a values for the ionization of the oxime functions, the rates of solvolysis of three *syn*-α-haloacetophenone oximes and *anti*-α-bromoacetophenone oxime (II), determined spectrophotometrically, have been found to obey the rate law shown in eq 1.[8] The second-order rate constants

$$v = k[\alpha\text{-halooxime}][OH^-] \quad (1)$$

obtained are in the following ratio: syn fluoro, 1.0; syn chloro, 2.9×10^3; syn bromo, 1.0×10^5; and anti bromo, 4.8×10^6.[9] The pH–rate profile for the solvolysis of the *syn*-fluorooxime is sigmoidal at high pH (9–13) with a dependency on a group ionizing with $pK_a = 10.5$, which we postulate to be the oxime function.[10] These findings indicate that ionization of the oxime function as well as loss of halide ion occur in steps which crucially affect the rate of reaction.

As described already for the reaction of I with morpholine buffer, the solvolyses of the *syn*-α-haloacetophenone oximes, as well as that of the anti species II, in various buffered aqueous solutions gave products of anti configuration, corresponding to replacement of the halogen with the buffer compound.[11] However, the rates of reaction are independent of the concentration of the buffer species.[12]

Addition of excess Br^- (0.5 *M*) decreases the rate of solvolysis of 8.4×10^{-5} *M* *syn*-α-bromooxime (I) 16-fold in 0.01 *M* acetate buffer at pH 5. The behavior of the anti isomer (II) in the presence of Br^- is quite different. When II (1.9×10^{-4} *M*) is solvolyzed in the absence of Br^- in pH 4, 0.01 *M* acetate buffer, for example, there is a first-order decrease in the absorbance at 260 nm ($t_{1/2}$ = 6 sec), corresponding to replacement of the bromide in the substrate by acetate. However, in the presence of 0.5 *M* Br^-, there is an increase in absorbance to a maximum value, reached after 3 min, followed by a slower decrease in absorbance. By carrying out this

(1) J. H. Smith, J. H. Heidema, E. T. Kaiser, J. B. Wetherington, and J. W. Moncrief, *J. Amer. Chem. Soc.*, **94**, 9274 (1972).
(2) Throughout this article, syn refers to the isomer having the alkyl group cis to the oxime oxygen; anti refers to the isomer having the alkyl group trans to the oxime oxygen.
(3) A. Dornow and H. D. Jordan, *Chem. Ber.*, **94**, 67, 76 (1961).
(4) W. Pritzkow, H. Schaefer, P. Papst, A. Ebenroth, and J. Beger, *J. Prakt. Chem.*, **29**, 123 (1965).
(5) H. P. Fischer and C. A. Grob, *Helv. Chim. Acta*, **45**, 2528 (1962).
(6) M. Masaki, K. Fukui, and M. Ohta, *J. Org. Chem.*, **32**, 3564 (1967).
(7) M. Ohno, S. Torimitsu, N. Naruse, M. Okamoto, and I. Sakai, *Bull. Chem. Soc. Jap.*, **39**, 1129 (1966), and earlier references therein.
(8) Below pH 2, the acid-catalyzed hydrolysis of the oxime function, resulting in α-halo ketone formation, becomes the primary reaction. The *syn*-α-halooximes were prepared from the corresponding α-haloacetophenones by reaction with hydroxylamine sulfate in methanol.
(9) These rate constants were determined from measurements in 0.1 *M* morpholine buffers containing 0.5 *M* KCl in the case of the syn fluoro compound, 0.05 *M* Tris buffers containing 0.5 *M* NaCl for the syn chloro, and 0.1 *M* acetate buffers for the syn and anti bromo compounds.
(10) The pK_a for the ionization of acetophenone oxime is 11.48 (R. P. Bell and W. C. E. Higginson, *Proc. Roy. Soc.*, **197**, 141 (1949)); a decrease of one unit in the pK_a due to the presence of the electron-withdrawing fluoro group would not be unreasonable.
(11) When unbuffered solutions are used (pH maintained with a pH-stat), the oxime function acts as a nucleophile to give a dimeric product.
(12) For example, a 40-fold increase in the concentration of morpholine at pH 9.0 resulted in an increase of only 10% in the observed rate constant for the solvolysis of I.