mm), mp 94–97°. Analysis showed 95% purity, 2% being I and 3% lower boiling unidentified materials. Recrystallization from pentane gave mp 98–99° (lit.[7a] mp 101°), semicarbazone mp 200–201° (lit.[7a] mp 200°). The precipitate, which had been set aside, was added to a mixture of 300 ml of saturated aqueous sodium carbonate and 200 ml of ethyl ether and stirred vigorously until solution had occurred. The ether layer was separated and the aqueous carbonate layer was extracted with two 50-ml ether portions. The ether portions were combined, dried over magnesium sulfate, and distilled to yield 42 g (28%) of *endo*-5,6-trimethylene-9-norbornanone (I), bp 132–134° (20 mm), mp 105–105.5°, semicarbazone mp 214–215°, dibenzylidene derivative mp 191–191.5° (lit.[6] semicarbazone mp 215°, dibenzylidene derivative mp 191°). *Anal.* Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 80.16; H, 9.57.

**Relative Rates of Oxidation of *endo*-5,6-Trimethylene-*exo*-9-norbornanol and the Exo-8 Isomer.**—A mixture of alcohols consisting of 9.75 mmol of *endo*-5,6-trimethylene-*exo*-9-norbornanol and 15.25 mmol of *endo*-5,6-trimethylene-*exo*-8-norbornanol, obtained by hydroboration of *endo*-5,6-trimethylene-8-norbornene, was treated wth 50% of the theoretical amount of chromic acid using the previously described procedure.[20] At the end of the reaction glpc analysis revealed that there remained 3.85 mmol of the 9-alcohol and 9.90 mmol of the 8-alcohol. According to the given procedure,[22] the rate of oxidation of the 9-alcohol relative to that of the 8 isomer was calculated to be 2.1.

**8,9-Dehydro- and 9,10-Dehydro-*endo*-5,6-trimethylene-*exo*-2-norbornanol (V). Method A. Hydroboration of *endo*-Dicyclopentadiene.**—To a well-stirred solution containing 198 g (1.5 mol) of *endo*-dicyclopentadiene in 250 ml of THF was added under a nitrogen atmosphere 167 ml (1 mol of hydride) of 1 *M* diborane solution in THF. The solution was allowed to become hot owing to an exothermic reaction. After addition was complete, the reaction mixture was stirred for 3 hr, and then 150 ml of 3 *N* sodium hydroxide was added, followed by the slow addition of 150 ml of 30% hydrogen peroxide, and stirred for 8 hr. The THF layer was salted out by adding potassium carbonate and separated. The aqueous phase was extracted with ether and the combined solution was dried over magnesium sulfate before the solvent was distilled off. The residue was distilled to give 72 g (0.55 mol) of the starting material, bp 70–75° (18 mm), 96 g (0.64 mol) of a mixture of monoalcohols, bp 124–130° (15 mm), and higher boiling diols. Analysis of the monoalcohol showed the presence of 37% 2-alcohol (V). A 1 *M* ether solution of this mixture of monoalcohols was extracted three times with a 1 *M* silver nitrate solution using $^2/_3$ the volume of silver nitrate each time as the total volume of ether solution. The aqueous portions were extracted once with ether and then back extracted once with silver nitrate solution. The combined ether solution was washed once with water and then dried over magnesium sulfate. The ether was distilled off at a reduced pressure to give a quantitative recovery of V.

**Method B. Oxymercuration–Demercuration[19] of *endo*-Dicyclopentadiene.**—Mercuric acetate (63.7 g, 0.2 mol) was dissolved in 200 ml of water and 200 ml of THF, and to the resulting yellow solution was added with stirring 26.4 g (0.2 mol) of *endo*-dicyclopentadiene. After the yellow color disappeared the mixture was stirred for an additional 10 min and cooled to *ca.* −10°. To this solution was added successively 200 ml of cold 3 *N* sodium hydroxide solution and 200 ml of cold basic sodium borohydride solution (0.5 *M* in borohydride and 3 *N* in sodium hydroxide). The mixture was stirred until mercury settled and the aqueous layer was separated and extracted with hexane. The combined organic solution was dried over magnesium sulfate and the solvent was removed under a reduced pressure. Analysis showed the presence of 91% alcohol and 9% acetate. The residue was then treated with lithium aluminum hydride in THF in order to reduce the small amount of acetate and, at the same time, to reduce any residual mercurial products which were found to interfere with the catalytic hydrogenation. The final product was isolated in the usual manner. Analysis showed that the reaction proceeded to the extent of 89.5%, the product being practically pure 2-alcohol (V).

***endo*-5,6-Trimethylene-*exo*-2-norbornanol.**—The mixture of 8,9-dehydro- and 9,10-dehydro-*endo*-5,6-trimethylene-*exo*-2-norbornanol (V) was reduced according to the previous procedure.[8] The product was recrystallized from pentane, mp 81.5–82.0° (lit.[7b] mp 80.5–81.5°).

***endo*-5,6-Trimethylene-2-norbornanone (III).**—*endo*-5,6-Trimethylene-*exo*-2-norbornanol was oxidized with use of the modified procedure developed in this laboratory.[20] The crude product, obtained in 95% yield, was essentially free of the starting material as shown by glpc analysis. The product was purified by sublimation, mp 102–104° (lit.[7b] mp 97–103°).

**Registry No.**—I, 19138-60-4; 8,9-dehydro-V, 36807-74-6; 9,10-dehydro-V, 36807-75-7; *endo*-dicyclopentadiene, 1755-01-7.

(22) R. Stewart, "Oxidation Mechanisms," W. A. Benjamin, New York' N. Y., 1964, p 39.

# Effects of Substituents on the Rates of Disproportionation of Substituted Phenylglyoxals in Alkaline Solution[1a,b]

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A series of meta- or para-substituted phenylglyoxals, including H, *p*-$CH_3$, *p*-$OCH_3$, *p*-Br, *p*-Cl, *p*-phenyl, *m*-$OCH_3$, *p*-$NO_2$, and *p*-OH, were examined for linear free energy relationships between chemical reactivity and substituent constants, and between chemical reactivity and carbonyl stretching frequencies of the ketone and aldehyde carbonyls. At pH 12, the hydroxide ion catalyzed disproportionation of the phenylglyoxals into the corresponding mandelic acids follows the Hammett relationship with $\rho$ 2.0, indicative of a transition state stabilized by electron-withdrawing groups. These rates of disproportionation also correlate quite well with the carbonyl stretching frequencies of the ketone carbonyls, both for the hydrated and the anhydrous phenylglyoxals. The aldehyde carbonyl stretching frequencies are essentially independent of ring substituents, $\nu_{C=O}$ 1727 ± 2 $cm^{-1}$. The disproportionation of $\alpha$-keto aldehydes is known to involve intramolecular hydride migration. The results of the present study suggest that hydride migration is the rate-determining step in the disproportionation of this series of substituted phenylglyoxals.

The glyoxalase system is composed of two enzymes: glyoxalase I, which utilizes glutathione (GSH) as co-enzyme and catalyzes the disproportionation of methylglyoxal into the thiol ester of lactic acid and GSH, and glyoxalase II, which hydrolyzes this thiol ester to regenerate GSH and liberate lactic acid.[2,3] Scheme I

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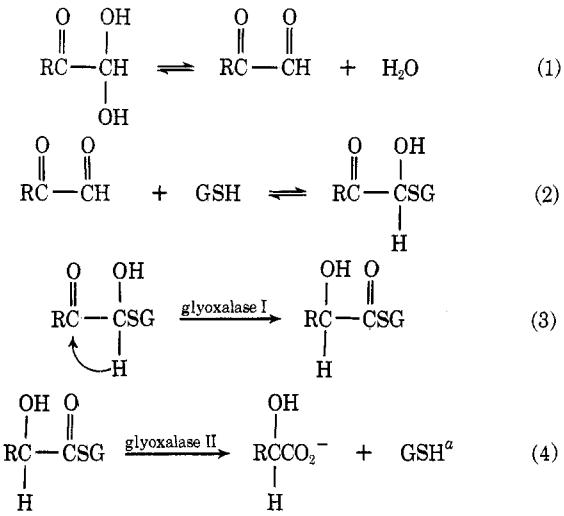
(2) E. Racker, *J. Biol. Chem.*, **190**, 685 (1951).

(3) Review article on glutathione and the glyoxalase system: W. E. Knox in "The Enzymes," Vol. 2, P. D. Boyer, H. Lardy, and K. Myrback, Ed., Academic Press, New York, N. Y., 1960, p 253.

SCHEME I



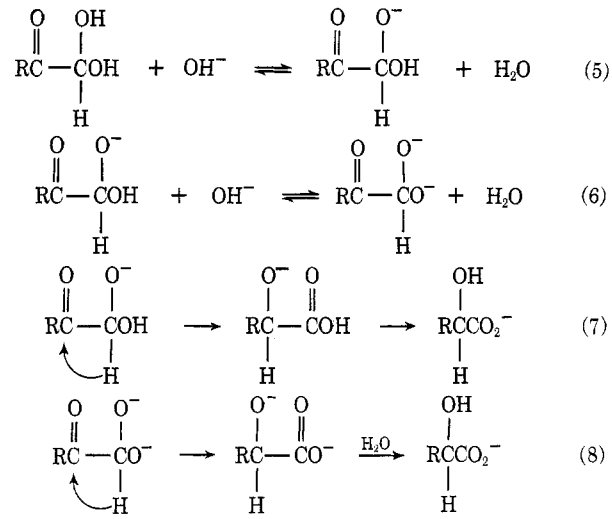
[a] GSH = γ-L-glutamyl-L-cysteinylglycine.

summarizes the reactions of the glyoxalase system. Reactions 1 and 2 of Scheme I are preenzymic reactions to form a hemimercaptal, which is the actual enzyme substrate.[4,5] The net reaction in the glyoxalase system is the conversion of an α-keto aldehyde into an α-hydroxycarboxylic acid. This is analogous to an intramolecular Cannizzaro reaction involving hydride migration from the aldehydic group to the α carbon. The glyoxalase I reaction (reaction 3 of Scheme I) is known to occur without solvent exchange of the aldehydic hydrogen,[6,7] as in the Cannizzaro reaction. The importance of the glyoxalase system is not yet clear. It is ubiquitous in nature, and there have been suggestions that the system may play an important role in the regulation of cell growth.[8] The general ability of methylglyoxal and other α-keto aldehydes to inhibit the growth of both bacteria and mammalian cells is well established[9,10] and has resulted in the specific suggestion that the glyoxalase system may function in a regulatory capacity by monitoring intracellular methylglyoxal (or other α-keto aldehydes) concentrations.[11]

The disproportionation of α-keto aldehydes in alkaline solution is also an intramolecular Cannizzaro reaction. This reaction has been studied extensively, especially for phenylglyoxal,[12-14] and also involves migration of the aldehydic hydrogen without exchange with solvent.[13] Furthermore, Hine and Koser[14] have established that the disproportionation of phenylglyoxal involves intramolecular hydride migration as the rate-determining step. A summary of their proposed reaction sequence is given in Scheme II. Comparison of the two reaction schemes shows the formal similarity

(4) E. E. Cliffe and S. G. Waley, *Biochem. J.*, **79**, 475 (1961).
(5) K. A. Davis and G. R. Williams, *Can. J. Biochem.*, **47**, 553 (1969).
(6) V. Franzen, *Chem. Ber.*, **89**, 1020 (1956).
(7) I. A. Rose, *Biochim. Biophys. Acta*, **25**, 214 (1957).
(8) A. Szent-Gyorgyi, *Science*, **149**, 34 (1965).
(9) L. G. Egyud and A. Szent-Gyorgyi, *Proc. Nat. Acad. Sci. U. S.*, **55**, 388 (1966).
(10) M. A. Apple and D. M. Greenberg, *Cancer Chemother. Rep.*, **51**, 455 (1967).
(11) A. Szent-Gyorgyi, L. G. Egyud, and J. A. McLaughlin, *Science* **155**, 539 (1967).
(12) E. R. Alexander, *J. Amer. Chem. Soc.*, **69**, 289 (1947).
(13) W. von E. Doering, T. I. Taylor, and E. F. Schoenewaldt, *ibid.*, **70**, 455 (1948).
(14) J. Hine and G. F. Koser, *J. Org. Chem.*, **36**, 3591 (1971).

SCHEME II



between the enzyme-catalyzed reaction (3) and the hydroxide-catalyzed reactions (7 and 8).

We have examined the effects of substituents on the hydroxide-catalyzed disproportionation of a series of substituted phenylglyoxals in order to (1) test whether reactions 7 and 8 involve rate-determining hydride migration for a broad series of meta or para substituents; (2) examine this reaction for linear free energy relationships between reactivity and substituent constants; (3) attempt to explain the observed reactivity by analyzing the carbonyl stretching frequencies of the aldehyde and ketone carbonyls; (4) obtain an understanding of reactions 7 and 8 as models for the glyoxalase I reaction. We recently observed that the glyoxalase I catalyzed disproportionation of substituted phenylglyoxals is insensitive to ring substituents.[15] This raises the question of whether reaction 3 involves rate-determining hydride migration or whether hydride migration simply shows a very small substituent effect. Reactions 7 and 8 thus become critical models for reaction 3.

## Results and Discussion

The rates of disproportionation of a series of substituted phenylglyoxal hydrates, including H, *p*-$CH_3$, *p*-$OCH_3$, *p*-Br, *p*-Cl, *p*-phenyl, *m*-$OCH_3$, and *p*-$NO_2$, were measured at pH 12 by following the changes in the uv absorbances at the $\lambda_{max}$ of the hydrates. *p*-Hydroxyphenylglyoxal was also examined. This member of the series disproportionated slowly at pH 12 and, consequently, was examined at higher pH. The *p*-$OCH_3$ derivative was also examined at this higher pH (*ca.* 0.1 *M* NaOH solution) and the factor $k_{p\text{-}OCH_3}/k_{p\text{-}O^-}$ = 39 was assumed valid at pH 12. The *p*-OH derivative exists as the *p*-$O^-$ anion at high pH. The pseudo-first-order rate constants obtained and the wavelengths employed are listed in Table I. There is a 3600-fold range in rate constants between the *p*-$NO_2$ and *p*-$O^-$ derivatives, indicative of transition-state stabilization by electron-withdrawing groups. Figure 1 shows a Hammett plot of log *k* *vs.* $\sigma_x$[16] for this series of com-

(15) D. L. VanderJagt, L-P. B. Han, and C. H. Lehman, *Biochemistry*, **11**, 3735 (1972).
(16) σ Values taken from J. Hine, "Physical Organic Chemistry," 2nd ed., McGraw-Hill, New York, N. Y., 1962, p 87.

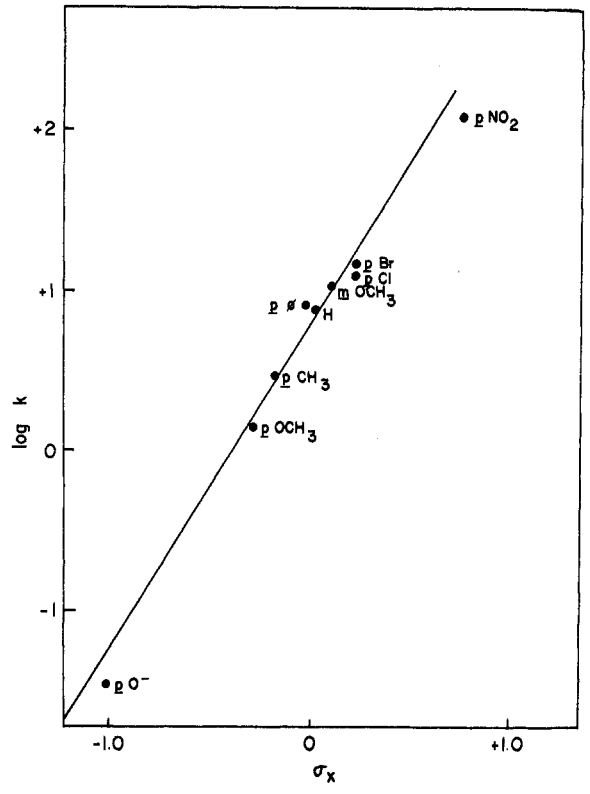



Figure 1.—Hammett plot of log $k$, the rate constants for the disproportionation of the substituted phenylglyoxals, pH 12, *vs.* $\sigma_x$. Slope, $\rho$, is 2.0.

TABLE I

RATE CONSTANTS FOR THE DISPROPORTIONATION OF SUBSTITUTED PHENYLGLYOXALS, pH 12, 25°[a]

| Registry no. | x | $k$, $10^{-4}$ sec$^{-1}$ | log $k$ | $\sigma_x$[c] | $\lambda$, nm[d] |
|---|---|---|---|---|---|
| 1074-12-0 | H | 7.60 ± 0.13 | 0.881 | 0.0 | 251 |
| 1075-47-4 | *p*-$CH_3$ | 3.05 ± 0.05 | 0.484 | −0.170 | 263 |
| 1076-95-5 | *p*-$OCH_3$ | 1.37 ± 0.04 | 0.137 | −0.268 | 287 |
| 5195-29-9 | *p*-Br | 13.9 ± 0.1 | 1.143 | +0.232 | 264 |
| 4998-15-6 | *p*-Cl | 12.2 ± 0.3 | 1.086 | +0.227 | 260 |
| 4974-58-7 | *p*-Ph | 7.91 ± 0.08 | 0.898 | −0.01 | 292 |
| 32025-65-3 | *m*-$OCH_3$ | 10.1 ± 0.1 | 1.004 | +0.115 | 255 |
| 4974-57-6 | *p*-$NO_2$ | 125 ± 5 | 2.097 | +0.778 | 268 |
| 24685-80-5 | *p*-$O^-$ | 0.035[b] | −1.46 | −1.00 | 284 |

[a] Rates measured spectrophotometrically in phosphate buffer, $\mu$ 0.6. [b] *p*-OH phenylglyoxal exists as the *p*-$O^-$ derivative at high pH. Since this substituted phenylglyoxal is quite stable at pH 12, it was disproportionated at higher pH along with the *p*-$OCH_3$ compound, and the factor *p*-$OCH_3$/*p*-$O^-$ = 39 was assumed applicable at pH 12. [c] Values for $\sigma_x$ obtained from ref 16. [d] $\lambda_{max}$ values of the substituted phenylglyoxal hydrates, pH 7. The rates of disproportionation were monitored at these wavelengths.

pounds. A fairly good linear free energy relationship is observed. The slope, $\rho$, is 2.0, comparable in size and magnitude to the $OH^-$-catalyzed hydrolysis of substituted methyl benzoates.[17] The linear relationship over this wide range of substituents suggests a common mechanism for this series of disproportionations.

In their study on the mechanism of disproportionation of phenylglyoxal hydrate, Hine and Koser[14] reported that the rate-determining step is the intramolecular hydride migration (reaction 7 or 8 of Scheme II) and that reaction 8 predominates at hydroxide concentrations above 3 m$M$. At pH 12, both the mono- and dianion should contribute to the observed rate with the majority of reaction occurring *via* the dianion. The existence of a linear relationship for the entire series of substituted phenylglyoxals examined in the present study at pH 12 can be explained if reaction 8 involving the dianion species is the major reaction taking place for all of the substituted phenylglyoxals examined. However, this would require that the acidities of the hydrates (*i.e.*, reactions 5 and 6 of Scheme II) show little or no sensitivity to substituents, so that at pH 12 the reactions primarily are the disproportionations of the dianions. Alternatively, the acidities of the hydrates could be sensitive to substituents, but reactions 7 and 8 could have identical sensitivities to substituents. This alternative seems unlikely. To examine whether the acidities of the hydrates are insensitive to substituents, the carbonyl stretching frequencies of the substituted phenylglyoxals were determined for the ketones in the hydrated compounds and for both the aldehydes and the ketones in the unhydrated compounds. The values are listed in Table II. The aldehyde carbonyl stretching

TABLE II

INFRARED CARBONYL STRETCHING FREQUENCIES OF THE KETONE AND ALDEHYDE CARBONYLS OF SUBSTITUTED PHENYLGLYOXALS AND THEIR HYDRATES

| | $\nu_{C=O}$, cm$^{-1}$ | | |
|---|---|---|---|
| Substituent | Ketone | Aldehyde | Ketone (hydrated series) |
| H | 1676 | 1727 | 1699 |
| *p*-$CH_3$ | 1674 | 1726 | 1688 |
| *p*-$OCH_3$ | 1666 | 1728 | 1681 |
| *p*-Br | 1680 | 1729 | 1695 |
| *p*-Cl | 1679 | 1729 | 1695 |
| *p*-Ph | 1673 | 1726 | 1694 |
| *m*-$OCH_3$ | 1674 | 1726 | 1693 |
| *p*-$NO_2$ | 1688 | 1729 | 1708 |
| *p*-OH | 1664 | 1728 | 1681 |

frequency is 1727 ± 2 cm$^{-1}$, totally insensitive to ring substituents, while the ketone carbonyls are quite sensitive to ring substituents, both for the hydrates and the unhydrated phenylglyoxals. If one assumes that the carbonyl stretching frequency reflects sensitivity to nucleophilic addition, one might expect that the extent of hydration of the aldehyde in aqueous solution and the p$K_a$ values of the hydrates will be similar for this entire series of phenylglyoxals. This would help explain the linear relationship observed in the rates of disproportionation at pH 12. This conclusion that the chemistry at the aldehyde group is insensitive to substituents agrees with earlier observations that the rates of addition of glutathione to the aldehyde groups of substituted phenylglyoxals (reaction 2, Scheme I) and the dissociation constants of the resulting hemimercaptals are insensitive to ring substituents.[15]

If hydride migration is rate determining, and if the ketone carbonyl stretching frequencies reflect the influence of the ring substituents, linear relationships might be expected in plots of log $k$ *vs.* $\nu_{C=O}$. Figures 2 and 3 show plots of log $k$ *vs.* the ketone carbonyl stretching frequencies of the hydrates and the unhydrated phenylglyoxals, respectively. Fairly good

(17) H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **78**, 815 (1959).

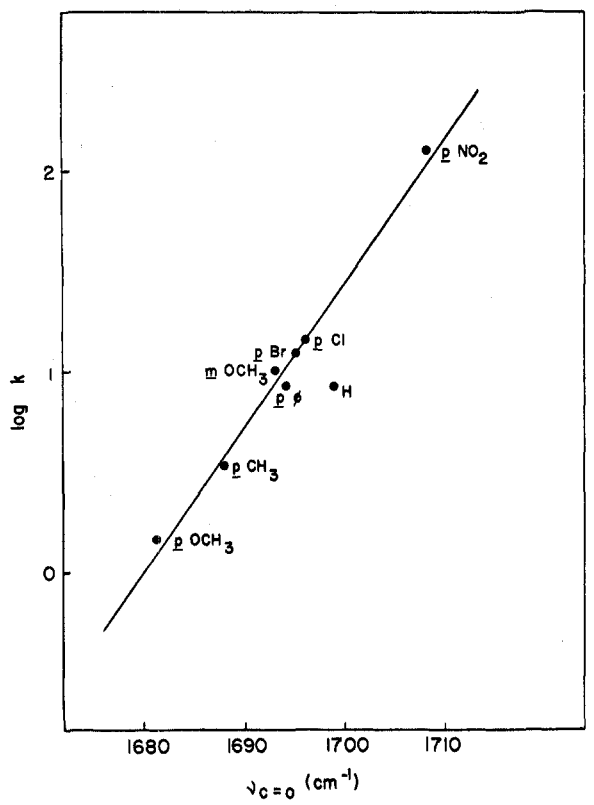



Figure 2.—Plot of log $k$, the rate constants for the disproportionation of the substituted phenylglyoxals, pH 12, *vs.* the ketone carbonyl stretching frequencies of the hydrated phenylglyoxals.

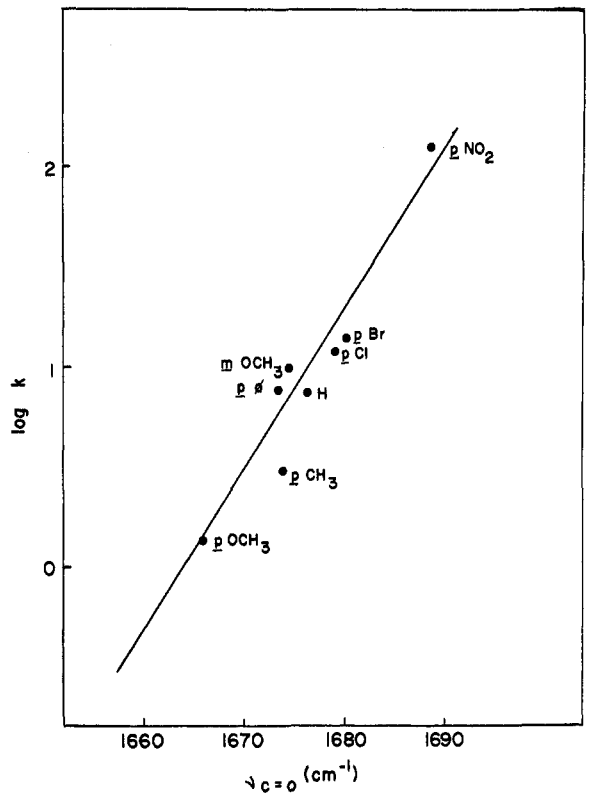



Figure 3.—Plot of log $k$, the rate constants for the disproportionation of the substituted phenylglyoxals, pH 12, *vs.* the ketone carbonyl stretching frequencies of the anhydrous phenylglyoxals.

linear free energy relationships are observed in both cases. The sensitivity of the reaction is about one log unit of $k$ for a $\Delta\nu_{C=O}$ of 13 $cm^{-1}$. These results agree with the general conclusion that the carbonyl stretching frequency can be a good indicator of chemical reactivity. Previous studies have shown that ketone carbonyl stretching frequencies can also be good models for predicting reactivities of ester solvolyses proceeding by carbonium ion intermediates.[18,19]

The usefulness of reaction 7 and 8 as models for the glyoxalase I reaction (reaction 3, Scheme I) is limited. The high sensitivity of the $OH^-$-catalyzed disproportionation of substituted phenylglyoxals to substituents compared to the lack of sensitivity[15] in the glyoxalase I reaction suggests that hydride migration may not be the rate-determining step in the enzyme reaction.

## Experimental Section

The substituted phenylglyoxals used in this study were synthesized by the following general procedures.

**Procedure A.**[20]—A substituted acetophenone as a 1–2 $M$ solution in dioxane containing an equivalent amount of selenous acid was refluxed for 4 hr. The mixture was concentrated by rotary evaporation, and the residue was vacuum distilled. The resulting oil was added to hot water to form the crystalline substituted phenylglyoxal hydrate, which was recrystallized from a mixture of chloroform and acetone.

**Procedure B.**[21]—A slurry of a substituted phenacyl bromide in acetonitrile was treated with a slight excess of $AgNO_3$. The resulting mixture was stirred for 24–48 hr at room temperature and filtered, and the solvent was removed by rotary evaporation. The residue (a phenacyl nitrate) was dissolved in diethyl ether and washed with water. After drying over $MgSO_4$, the solvent was removed, and the residue was added to dimethyl sulfoxide containing about 1% sodium acetate. The mixture was stirred at room temperature for 30 min and then was poured into ice–water saturated with NaCl. The resulting mixture was extracted with diethyl ether, washed with water, and dried over $MgSO_4$, and then the solvent was evaporated off. The resulting substituted phenylglyoxal hydrate was recrystallized as in procedure A.

The substituted phenylglyoxal hydrates prepared by either procedure were colorless solids except for the $p$-$NO_2$ derivative, which did not form a crystalline hydrate. The melting points, however, were observed to be somewhat variable during the recrystallization procedures. This presumably is a reflection of the extent of hydration and has also been observed by others.[14] All of the substituted phenylglyoxals were converted into the dioxime derivatives for elemental analysis. The data for characterization of the series of phenylglyoxals are given in Table III.

**Rates of Disproportionation.**—Phosphate buffers, pH 12, $\mu$ 0.6, were prepared by adding KOH to solutions of $Na_2HPO_4$ in distilled, deionized water. The ionic strength was due entirely to the buffer species. The pH measurements were made on a Sargent Welch Model DR pH meter with a glass electrode. Reaction rates were monitored at the $\lambda_{max}$ values of the substituted phenylglyoxals obtained from uv spectra recorded in pH 7 phosphate buffer using a Cary 15 recording spectrophotometer. In all cases, the substituted phenylglyoxals have molar extinction coefficients of *ca.* $10^4$ $M^{-1}$ $cm^{-1}$ at the $\lambda_{max}$ whereas the substituted mandelate products show low absorption at these wavelengths. The reaction rates were measured on a Gilford 222 recording spectrophotometer employing Beckman DU optics. The temperature was controlled (±0.2°) with a circulating water bath. First-order rate constants were obtained from computer-calculated least squares slopes of plots of log absorbance change *vs.* time. Correlation coefficients were generally better than 0.999. Reactions were initiated by addition of small quantities (10-20 $\mu$l) of 1:1 ethanol–$H_2O$ stock solution of the substituted phenylglyoxals. These small quantities were placed on the end of a flattened stirring rod and introduced directly into the spectrophotometer cell containing 3.0 ml of temperature-equilibrated buffer. The ethanol was generally useful for preparing stock

(18) C. S. Foote, *J. Amer. Chem. Soc.*, **86**, 1853 (1964).
(19) P. v. R. Schleyer, *ibid.*, **86**, 1854 (1964).
(20) H. A. Riley and A. R. Gray, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 509.
(21) N. Kornblum and H. W. Frazier, *J. Amer. Chem. Soc.*, **88**, 865 (1966).

TABLE III
CHARACTERIZATION OF SUBSTITUTED PHENYLGLYOXALS

| Substituent | Synthetic procedure | Mp of hydrate, °C | Mp of dioxime, °C | Elemental analysis of dioxime, % C | H | N |
|---|---|---|---|---|---|---|
| H | A | 76-77 | 174-176 | 58.53 | 4.91 | 17.06 calcd |
| | | | | 58.70 | 5.10 | 17.04 obsd |
| *p*-$CH_3$ | A | 98-99 | 166.5-168.2 | 60.67 | 5.66 | 15.96 |
| | | | | 60.81 | 5.63 | 15.87 |
| *p*-$OCH_3$ | B | 126-127.5 | 152-153 | 55.67 | 5.19 | 14.43 |
| | | | | 55.85 | 5.14 | 14.26 |
| *p*-Br | B | 133.5-134.9 | 167.5-168.5 | 39.53 | 2.90 | 11.52 |
| | | | | 39.74 | 3.14 | 11.39 |
| *p*-Cl | B | 120-122 | 159-160 | 48.38 | 3.55 | 14.10 |
| | | | | 48.28 | 3.73 | 14.33 |
| *p*-Ph | B | 116-118 | 216-218 | 69.99 | 5.03 | 11.66 |
| | | | | 70.02 | 4.94 | 11.59 |
| *m*-$OCH_3$ | B | 77-78.5 | 163.5-164.8 | 55.67 | 5.19 | 14.43 |
| | | | | 55.73 | 5.10 | 14.55 |
| *p*-$NO_2$ | A | 131-132 (3 mm)[a] | 186-188 | 45.94 | 3.37 | 20.09 |
| | | | | 45.92 | 3.54 | 20.40 |
| *p*-OH | A | 86.5-87.5 | 190-193 | 53.33 | 4.48 | 15.55 |
| | | | | 53.15 | 4.73 | 15.86 |

[a] Boiling point of *p*-$NO_2$ derivative.

solutions of convenient concentrations. Use of stock solutions without ethanol gave the same rate data. The initial concentrations of substituted phenylglyoxals in the reaction cell were generally *ca.* $10^{-4}$ *M*.

**Carbonyl Stretching Frequencies.**—The ketone and aldehyde carbonyl stretching frequencies were measured on a Perkin-Elmer 621 recording spectrophotometer using very slow scan rates and expanded scales. Generally, the range 1800–1600 $cm^{-1}$ was scanned over a 1-hr period, and a polystyrene standard was added to the cell holder immediately after the carbonyl band was passed in order to accurately locate the carbonyl stretching frequency. This procedure gave values reproducible to ±1.5 $cm^{-1}$.

The ketone carbonyl stretching frequencies of the substituted phenylglyoxal hydrates were measured in Nujol mulls. The ketone and aldehyde carbonyl stretching frequencies of the unhydrated compounds were determined in dilute acetonitrile solutions. Although carbonyl frequencies are generally measured in carbon tetrachloride solutions, it was found that the unhydrated phenylglyoxals in carbon tetrachloride rapidly deteriorate, presumably by polymerization. Only a trace of water is required to initiate polymerization. Acetonitrile solutions were sufficiently stable to allow slow scanning rates to be used. The anhydrous solutions were prepared by warming acetonitrile solutions of the hydrates over molecular sieves, with repeated transfers to fresh molecular sieves.

# Dehydrogenation of α-(Phenylthio)cyclohexanone Accompanying Oxime Formation

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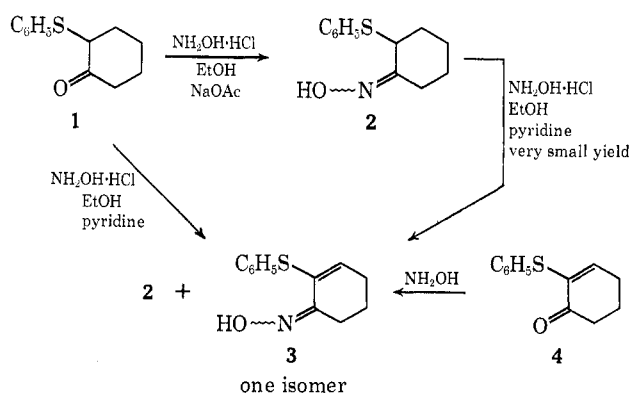
Treatment of **1** with hydroxylamine hydrochloride in ethanol–pyridine gave **3**. Compound **3** is the product of a novel oxidation–reduction reaction in the course of which a new carbon–carbon double bond is introduced.

In the course of the reaction of 2-(phenylthio)cyclohexanone (**1**) with hydroxylamine hydrochloride we have made the following observations. When the reaction was run with ethanol as the solvent and sodium acetate as the base the expected product, oxime **2**, was obtained as a mixture of *Z* and *E* isomers. On the other hand, with ethanol as the solvent and pyridine as the base, oxime **2** was obtained accompanied by an additional product **3**, clearly a result of an oxidation–reduction process. Treatment of oxime **2** under the conditions for the conversion of **1** to **3** produced very little of **3**. The resulting mixture was subjected to gc and mass spectral analysis of the TMS derivatives (*cf.* Experimental Section) and it was shown that less than 5% of **3** was produced by this route.




The structure of **3** was supported by (a) the nmr spectrum, which was compatible with the presence of one vinyl proton adjacent to a methylene group, and (b) the mass spectrum, which showed a molecular ion at *m/e* 219. The TMS derivative of **3** showed a molecular ion at *m/e* 291, which clearly indicated that **3** is a dehydro derivative of **2**. When the mass spectra of **2** and **3** were compared it was realized that the loss of the radical $C_6H_5S\cdot$ from the molecular ion leads to the most intense ion *m/e* 112 ($M^+ - C_6H_5S\cdot$) in the case of **2**. This loss is a minor process in the case of **3**; the intensity of the *m/e* 110 ion ($M^+ - C_6H_5S\cdot$) was less than 8% of the base peak. This observation