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Keto-Enol Equilibrium Constants of Simple Monofunctional Aldehydes and Ketones in Aqueous Solution

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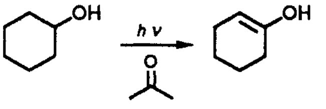
Abstract: Keto-enol equilibrium constants, K_E, were determined for five aliphatic ketones (2-butanone, 3-methyl-2-butanone, 3,3-dimethyl-2-butanone, 3-pentanone, and 2,4-dimethyl-3-pentanone) and three alicyclic ketones (cyclopentanone, cyclohexanone, and cycloheptanone) in aqueous solution at 25 °C by combining acid-catalyzed enolization and ketonization rate constants according to the relationship $K_E = k_E/k_K$. Enolization rate constants were measured by halogen scavenging and ketonization rate constants were measured by monitoring the decay of enols generated flash photolytically through photooxidation of the corresponding alcohols. The effects of structure on K_E, k_E, and k_K are discussed.

Enols are essential intermediates in many reactions of simple aldehydes and ketones, and the chemistry of simple enols is consequently of considerable importance. The magnitude of keto-enol equilibrium constants (K_E, eq 1) is of fundamental significance in this respect. These constants have traditionally been determined by the halogen titration method, invented by Meyer nearly a century ago.[1] This technique works well when enol contents are high, as for example in the case of β-dicarbonyl compounds,[2] but it fails badly when enol contents are low, as is the case for most simple monofunctional aldehydes and ketones.

(1)

In such situations it is useful to employ a kinetic method of determining K_E, which is based upon the fact that an equilibrium constant for any reaction is equal to the rate constant for the process in the forward direction divided by that for the process in the reverse direction. Thus, $K_E = k_E/k_K$ where k_E and k_K are enolization and ketonization rate constants, respectively. Values of k_E are easily obtained, for example by scavenging the enol as it is formed from the keto isomer. Measurement of k_K presents somewhat more of a problem, for it requires generating the usually quite labile enol in greater than equilibrium amount under conditions where its rate of ketonization may be determined accurately.

We have recently developed a number of methods for accomplishing this and have applied them to the study of enol chemistry.[3] Flash photolytic oxidation of alcohols by photoexcited acetone or acetaldehyde, eq 2, has proven to be especially useful in this respect. We have employed this method to determine the enol contents of a variety of simple aliphatic aldehydes and ketones and have published our results in preliminary form.[4] We now describe that work in full.



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Experimental Section

Materials. 3,3-Dimethyl-2-butanol was prepared by the sodium borohydride reduction of 3,3-dimethyl-2-butanone. All other materials were best available commercial grades. The alcohols and ketones were fractionally distilled before use. Solutions were made with deionized water purified further by distillation.

Kinetics of Enolization. Rates of enolization were measured by bromine scavenging under zero-order conditions. The reaction solutions contained 0.10 M bromide ion, which caused a constant fraction of the bromine to be complexed as the tribromide ion ($[Br_2]/[Br_3^-] = 0.6$), and the bromine concentration was monitored by measuring the absorbance of Br_3^- at either $\lambda = 320$ nm ($\epsilon = 5520$ M^{-1} cm^{-1}) or $\lambda = 330$ nm ($\epsilon = 2870$ M^{-1} cm^{-1}). Initial stoichiometric bromine concentrations were ca. 3×10^{-4} M, and ketone concentrations were ca. 2×10^{-2} M; reactions were followed to ca. 1% consumption of ketone.

In a typical run, 3.0 mL of an aqueous solution of ketone, sodium bromide, and hydrobromic acid contained in a cuvette was allowed to equilibrate with the thermostated cell compartment of the spectrophotometer (Cary 118). The reaction was then initiated by adding 5-10 μL of aqueous bromine solution and continuous absorbance recording was begun. Traces of absorbance versus time were accurately linear. First-order rate constants were calculated from the slopes of these traces, $\Delta A/\Delta t$, according to eq 3 in which K_{ass} (= 17 M)[5] is the equilibrium constant for the bromine plus bromide ion association reaction; ketone concentrations, [K], were determined by weight or by spectrophotometric assay prior to the addition of bromine.

$$k_{obs} = (\Delta A/\Delta t)(1 + K_{ass}^{-1}[Br^-]^{-1})/[K]\epsilon_{Br_3^-} \qquad (3)$$

Product Determination. Two of the ketones investigated here can each enolize in two different directions to give regioisomeric enols that will produce different bromination products. Knowledge of the product ratios allows separation of global observed rates of enolization into regioisomeric components, and these product ratios were therefore determined in the following way.

The bromination was carried out on a large scale by allowing a 1-L amount of 0.10 M aqueous hydrobromic acid solution containing 0.02 M ketone and 0.008 M bromine to react in a water bath maintained at 25 °C. After a time judged to be sufficient to consume most of the bromine, the reaction was stopped by adding sodium bisulfite and the resulting solution was promptly extracted with 100 mL of dichloromethane. The bromination product ratio in this extract was then determined by analytical gas chromatography. The products were also identified and the ratio was verified by evaporating the solvent from the extract and subjecting the residue to ^1H NMR spectroscopy.[6]

Kinetics of Ketonization. Flash photolysis was performed in an apparatus of conventional design whose specifications have been described.[7] Enols were generated by photooxidation of appropriate alcohols, using either acetaldehyde or acetone as the oxidant, and ketonization was monitored by following the decrease in intensity of the strong enol absorbance in the region $\lambda = 205$-220 nm. Both alcohol and acetaldehyde or acetone concentrations in the reaction solutions were of the order of 0.1 M.

In a typical experiment, 10 mL of a solution of perchloric acid plus enough sodium chloride to bring the ionic strength up to 0.10 M, contained in a 10-cm jacketed cuvette maintained at 25.0 ± 0.1 °C, was purged of oxygen by nitrogen or argon bubbling. Appropriate amounts of alcohol and acetaldehyde or acetone were then added and, after the solution had reached temperature equilibrium with the cuvette, flash photolysis was effected. It was found that the photoreaction was not very

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[1] Meyer, K. *Justus Liebigs Ann. Chem.* **1911**, *380*, 212-242.

[2] See, e.g.: Wheland, G. W. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1960; pp 681-695.

[3] Kresge, A. J. *CHEMTECH* **1986**, *16*, 250-254; *Acc. Chem. Res.* **1990**, *23*, 43-48.

[4] Keeffe, J. R.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1988**, *110*, 1993-1995.

[5] Griffith, R. O.; McKeown, A.; Winn, A. G. *Trans. Faraday Soc.* **1932**, *28*, 101-107.

[6] Detailed data are available from: Schepp, N. P., Ph.D. Thesis, University of Toronto, 1989.

[7] Chiang, Y.; Hojatti, M.; Keeffe, J. R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 4000-4009.

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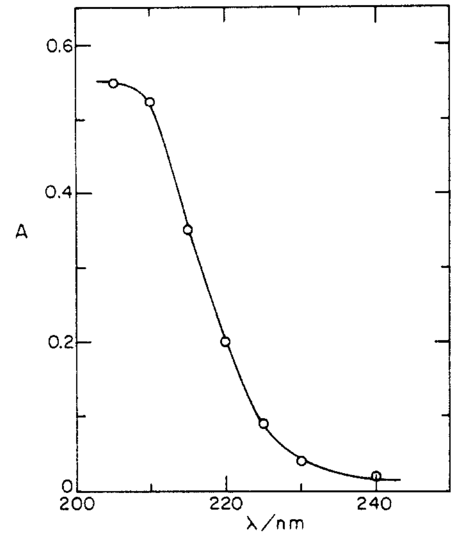


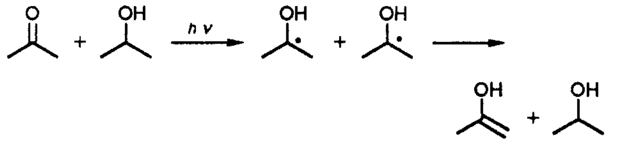
Figure 1. Ultraviolet spectrum of acetone enol generated by flash photolysis of a solution of 0.17 M isopropyl alcohol and 0.07 M acetone in 0.10 M aqueous perchloric acid at 25 °C.

efficient and the same solution could consequently be flashed a number of times; in most cases, 4–10 such replicate determinations were made.

Observed first-order rate constants were obtained by fitting the data to single or double exponential functions, as required, by a nonlinear least-squares routine.[8]

Results

Characterization of the Photooxidation Process. The photooxidation–reduction of alcohol and aldehyde or ketone pairs is a well-known process,[9a] and there is CIDNP evidence that the ketyl radicals so formed undergo disproportionation to give enols, eq 4.[10] We have added to this evidence by observing that flash photolysis of a solution of isopropyl alcohol and acetone produces a short-lived transient species that decays with a rate law identical with that for the ketonization of acetone enol[7,11] (vide infra). We also constructed a UV spectrum of this transient by performing flash photolysis experiments at different monitoring wavelengths and extrapolating the data to zero time. This spectrum, shown in Figure 1, consists of a strong band with $\lambda_{max} \leq 205$ nm (the low wavelength limit of our apparatus) and shows no absorbance above $\lambda \cong 230$ nm, as expected for an isolated carbon–carbon double bond bearing a hydroxyl group substituent; this spectrum is also similar to that of the corresponding ethyl vinyl ether.[12]



(4)

Additional support for identificaion of this transient as the enol of acetone comes from the manner in which its yield depends upon the concentration of isopropyl alcohol. A reaction scheme for the formation of acetone enol from triplet acetone, T*, is given in eq 5, where k_p is the rate constant for formation of enol by reaction of the triplet with isopropyl alcohol, k'_p is the rate constant for formation of enol by reaction of the triplet with other substances, e.g. the solvent, and k_d is the rate constant for decay of the triplet by all other processes. The quantum yield for enol formation is then given by eq 6, in which Φ_{ISC} (~1)[9b] is the quantum yield

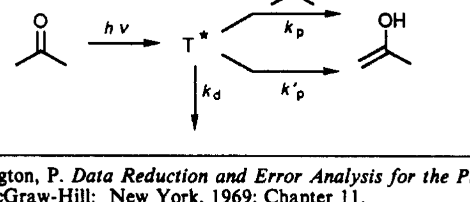
$$\Phi_E = \frac{k_p[i\text{-PrOH}] + k'_p}{k_p[i\text{-PrOH}] + k'_p + k_d}\Phi_{ISC} \qquad (6)$$

for intersystem crossing, and the ratio of quantum yields in the presence and absence of isopropyl alcohol is given by eq 7. This expression has the form of eq 8, where A/A_0, which is equal to $\Phi_E/(\Phi_E)_0$ and was used to measure this quantity, is the ratio of

$$\frac{\Phi_E}{(\Phi_E)_0} = 1 + \frac{[i\text{-PrOH}]}{(k'_p/k_d)[i\text{-PrOH}] + (k'_p + k_d)(k'_p/k_pk_d)} \qquad (7)$$

$$\frac{A}{A_0} = 1 + \frac{[i\text{-PrOH}]}{a[i\text{-PrOH}] + b} \qquad (8)$$

zero-time absorbances provided by flash photolysis experiments conducted at a fixed monitoring wavelength ($\lambda = 210$ nm) and constant acetone concentration (0.050 M).



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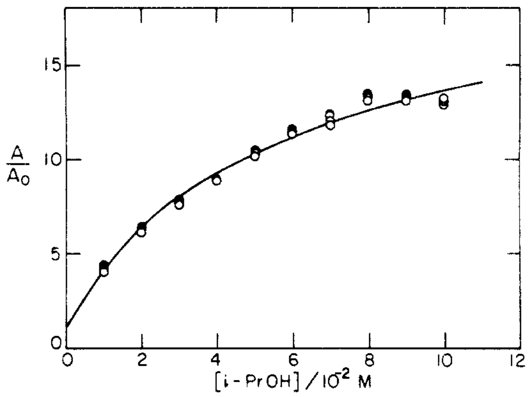

Figure 2. Relationship between isopropyl alcohol concentration and relative yield of acetone enol produced by photooxidation in aqueous solution.

This relationship predicts that the dependence of A/A_0 upon [*i*-PrOH] will be nonlinear, and Figure 2 shows that this is in fact the case and that the data[6] fit this model well: least-squares analysis provided the values $a = (5.05 \pm 0.15) \times 10^{-2}$ and $b = (2.81 \pm 0.09) \times 10^{-3}$ M, with which the line in Figure 2 was drawn. These results, when combined with the lifetime of triplet acetone in aqueous solution, τ (= $(k'_p + k_d)^{-1}$ = 20 ± 2 μs,[13] provide values of the three rate constants defined by eq 5: $k_p = (8.9 \pm 1.0) \times 10^5$ M^{-1} s^{-1}, $k'_p = (2.4 \pm 0.1) \times 10^3$ s^{-1}, and $k_d = (4.8 \pm 0.2) \times 10^4$ s^{-1}. The first of these is consistent with the rate constant reported for quenching of triplet acetone by isopropyl alcohol in acetonitrile solution, $k = (9.7 \pm 0.14) \times 10^5$ M^{-1} s^{-1}.[13] That plus the good adherence of these data to the model of eq 5 shown in Figure 2 reinforces identification of the process under examination as photooxidation of isopropyl alcohol by acetone.

Enolization. Rates of enolization of five aliphatic ketones and three alicyclic ketones were measured in aqueous hydrobromic acid solutions. For all substrates, measurements were made at five different acid concentrations over the range [HBr] = 0.02–0.10 M, and ionic strength was kept constant by adding sodium bromide as required. In all cases, observed first-order rate constants were accurately proportional to acid concentration, and linear least-squares analysis of the data[6] gave hydronium ion catalytic coefficients, $k^{E}_{H^+}$, which are summarized in Table I.

Two of the ketones examined, 2-butanone and 3-methyl-2-butanone, may each enolize in two different directions and give regioisomeric bromination products, eq 9. Examination of the

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(8) Bevington, P. *Data Reduction and Error Analysis for the Physical Sciences*; McGraw-Hill: New York, 1969; Chapter 11.

(9) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings Publ. Co.: Menlo Park, CA, 1978; (a) Chapter 10; (b) p 181.

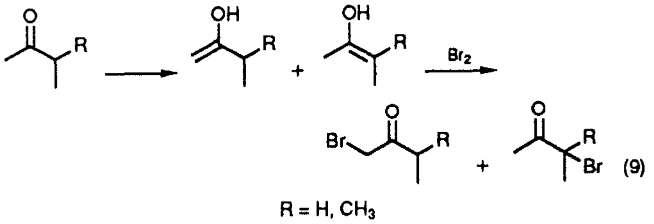
(10) Blank, B.; Henne, A.; Laroff, G. P.; Fischer, H. *Pure Appl. Chem.* **1975**, *41*, 475–494.

(11) Chiang, Y.; Kresge, A. J.; Tang, Y. S.; Wirz, J. *J. Am. Chem. Soc.* **1984**, *106*, 460–462.

(12) Sherrill, M. L.; Walter, G. F. *J. Am. Chem. Soc.* **1936**, *58*, 742–745.

(13) Porter, G.; Dogra, S. K.; Loufty, R. O.; Sugamori, S. E.; Yip, R. W. *J. Chem. Soc., Faraday Trans. I* **1973**, *69*, 1462–1474.

products by proton NMR showed that this did in fact occur in



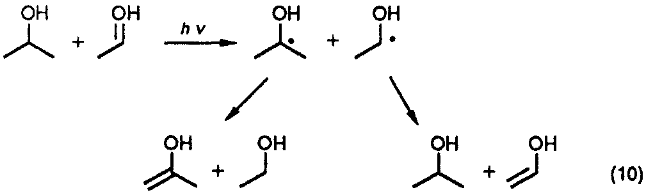
(9)

both cases. The product mixtures were therefore subjected to quantitative analysis (GC and NMR) and the following ratios were obtained: [1-bromo-2-butanone]/[3-bromo-2-butanone] = 0.419 ± 0.012 and [1-bromo-3-methyl-2-butanone]/[3-bromo-3-methyl-2-butanone] = 1.36 ± 0.02. These product ratios were then used to separate the overall rates of enolization for these two ketones into the regioisomeric components listed in Table I.

Ketonization of Acetone Enol. Rates of ketonization of the enol of acetone generated by flash photolytic photooxidation of isopropyl alcohol by acetone were determined in aqueous perchloric acid solutions over the concentration range [$HClO_4$] = 0.002–0.10 M at constant ionic strength (0.10 M). The data obeyed the first-order rate law well, and Figure 3 shows that observed first-order rate constants were accurately proportional to acid concentration. Least-squares analysis gave the hydronium ion catalytic coefficient $k^{K}_{H^+} = (5.48 \pm 0.06) \times 10^3$ M^{-1} s^{-1}.[6] This is in excellent agreement with the value obtained for acetone enol generated by Norrish type II photoelimination, $k^{K}_{H^+} = (5.38 \pm 0.08) \times 10^3$ M^{-1} s^{-1}.[7]

Measurements of the rate of ketonization of acetone enol generated by photooxidation of isopropyl alcohol with acetone were also made in D_2O solutions of DCl. The acid concentration was varied over the range [DCl] = 0.002–0.009 and ionic strength was maintained at 0.10 M. Once again, observed first-order rate constants were accurately proportional to acid concentration, and least-squares analysis gave the catalytic coefficient $k^{K}_{D^+} = (1.56 \pm 0.02) \times 10^3$ M^{-1} s^{-1}. Combination of this result with the value obtained in H_2O gives the isotope effect $k_{H^+}/k_{D^+} = 3.51 \pm 0.06$. A value of $k_{H^+}/k_{D^+} = 3.7$ has been estimated for this reaction from enolization rate measurements conducted by halogen scavenging at sufficiently low halogen concentrations to make the scavenging reaction partly rate determining.[14] Extraction of this isotope effect from the data required the assumption that the scavenging step was an encounter-controlled process, an assumption now known to be not quite correct;[15] nevertheless, the result obtained is consistent with the present directly determined isotope effect. Both values are of the magnitude expected for rate-determining proton transfer from the hydronium ion to carbon, which is the mechanism by which enols are known to ketonize.[7,16]

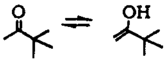
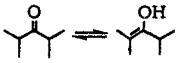
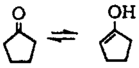
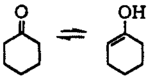
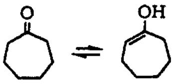
The enol of acetone was also generated here by photooxidation of isopropyl alcohol with acetaldehyde as the triplet oxidant. This process will produce two different ketyl radicals that may disproportionate in two different ways, giving the enol of acetaldehyde in addition to that of acetone, eq 10. These two enols can be



(10)

expected to ketonize at quite different rates, and, as Figure 4 shows, two transients with lifetimes differing by two orders of magnitude were in fact observed. Because these lifetimes were so different, data for decay of each transient could be fitted to the first-order rate law separately; each decay gave good first-order behavior. These experiments were done over a range of perchloric acid concentrations, [$HClO_4$] = 0.01–0.10 M, at constant ionic strength (0.10 M). Observed first-order rate constants in both

Table I. Summary of Rate Constants for Acid-Catalyzed Enolization and Ketonization in Aqueous Solution at 25 °C[a]

system	$k^{E}_{H^+}/10^{-5}$ M^{-1} s^{-1}	$k^{K}_{H^+}/10^{3}$ M^{-1} s^{-1}
	1.09±0.03	6.30±0.12
	1.47±0.02	5.93±0.09
	1.31±0.02	7.51±0.15
	2.59±0.04	0.839±0.018
	1.08±0.01	0.233±0.006
	2.92±0.04	0.793±0.022
	0.296±0.016	0.0975±0.0037
	6.07±0.10	5.30±0.04
	23.8±0.50	0.577±0.015
	3.98±0.07	4.02±0.09

[a] Ionic strentgh = 0.10 M.

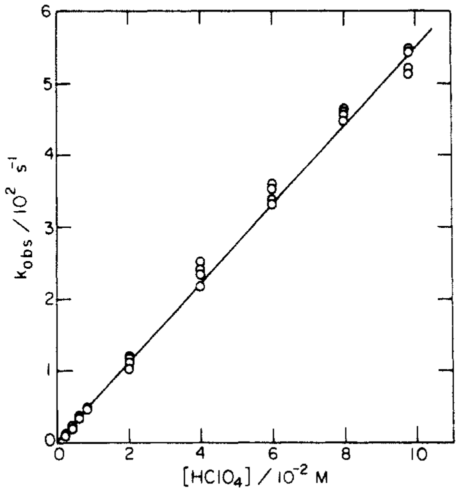


Figure 3. Relationship between perchloric acid concentration and rates of ketonization of acetone enol generated by photooxidation of isopropyl alcohol in aqueous solution at 25 °C.

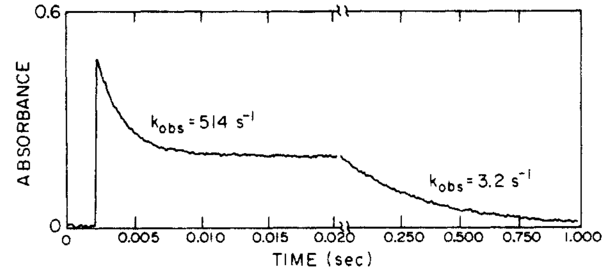


Figure 4. Time-dependent absorbance produced by flash photolysis of isopropyl alcohol and acetaldehyde in 0.10 M aqueous $HClO_4$ at 25 °C.

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(14) Toullec, J.; Dubois, J. E. *J. Am. Chem. Soc.* **1974**, *96*, 3524–3532.

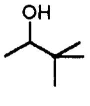
(15) Hochstrasser, R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1988**, *110*, 7875–7876.

(16) (a) Chiang, Y.; Kresge, A. J.; Walsh, P. A. *J. Am. Chem. Soc.* **1986**, *108*, 6314–6320. (b) Keeffe, J. R.; Kresge, A. J. In *The Chemistry of Enols*; Rappoport, Z., Ed.; Wiley: New York, Chapter 7; in press.

sets were accurately proportional to acid concentration, and least-squares analysis gave the hydronium ion catalytic coefficients $k^{K}_{H^+} = (5.68 \pm 0.29) \times 10^3$ M^{-1} s^{-1} and $(3.23 \pm 0.14) \times 10^1$ M^{-1} s^{-1}. The first of these values agrees well with the known rate constant for the ketonization of acetone enol, $k^{K}_{H^+} = (5.38 \pm 0.08) \times 10^3$ M^{-1} s^{-1},[7] and the second agrees with that for ketonization of acetaldehyde enol, $k^{K}_{H^+} = (3.30 \pm 0.14) \times 10^1$ M^{-1} s^{-1}.[7]

Ketonization of Other Enols. A number of other enols were also generated by photooxidation of appropriate alcohols with either acetone or acetaldehyde as the oxidant. In all cases at least two transient species were observed, one of which could be identified by its rate of decay as being the enol of either acetone or acetaldehyde. The particular oxidant chosen for a given experiment was selected to provide a sufficiently large reactivity difference between its enol and the other transients to allow good resolution of the various decays into separate components.

Eight different alcohol substrates were used: 3,3-dimethyl-2-butanol (**1**); 2,4-dimethyl-3-pentanol (**2**); cyclopentanol (**3**); cyclohexanol (**4**); cycloheptanol (**5**); 3-methyl-2-butanol (**6**); 3-pentanol (**7**); and 2-butanol (**8**). The first five of these can produce only one enol, in addition to that derived from the oxidant, and assignment of rate constants to individual transient species formed in their photooxidation was straightforward. The ketyl radical derived from 3,3-dimethyl-2-butanol (**1**) can lose hydrogen in only one direction, eq 11, and it can therefore give only one enol. The ketyl radicals derived from 2,4-dimethyl-3-pentanol (**2**) and the cyclic alcohols (**3**–**5**), on the other hand, can each lose hydrogen in two different directions, but these radicals are symmetrical and the two directions are equivalent, and again only a single enol can be formed from each radical.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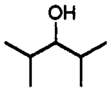
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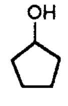
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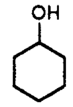
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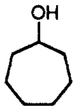
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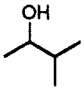
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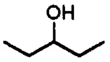
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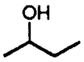
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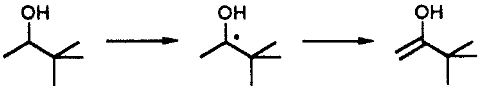
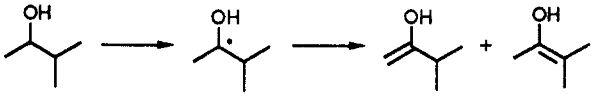
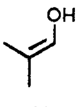

(11)

Photooxidation of the remaining three alcohols is less simple. The ketyl radical derived from 3-methyl-2-butanol (**6**) can disproportionate in two nonequivalent directions, eq 12, giving rise to two different enols, 3-methyl-1-buten-2-ol (**9**) and 3-methyl-2-buten-2-ol (**10**). Two transients, in addition to the enol derived from the oxidant, were in fact seen in the photooxidation of this alcohol. These two transients differed considerably in their rates of decay and, since β-methyl substitution is known to retard the rate of enol ketonization (the enol of isobutyraldehyde, **11**,[16a] is less reactive than that of acetaldehyde, **12**,[7] and the enol of isobutyrophenone, **13**,[17] is less reactive than that of acetophenone, **14**),[18] the faster decay was assigned to **9** and the slower to **10**.


(12)

9 **10**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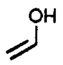
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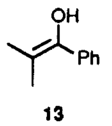
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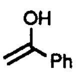
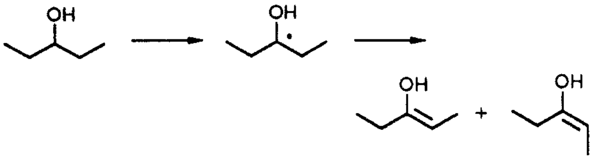
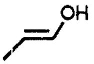

14

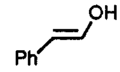
The ketyl radical formed from 3-pentanol (**7**) is symmetrical and will give only one regioisomeric enol, eq 13, but in this case cis and trans stereoisomers are possible. Examination of hydrogen loss from this ketyl by CIDNP shows that the cis and trans isomers are formed in equal amount in acetonitrile solution,[10] and it is likely that both are formed in comparable amount in the present aqueous medium as well. We were unable, however, to observe more than one transient decay, in addition to that attributable to the enol derived from the oxidant, in the flash photolytic photooxidation of 3-pentanol. It is likely, on the other hand, that the expected cis and trans enols differ little in reactivity: *cis*-1-propenol (**15**), for example, is only 1.5 times more reactive than *trans*-1-propenol (**16**),[19] and *cis*-2-phenylethenol (**17**) is only 2.5 times more reactive than *trans*-2-phenylethenol (**18**).[20] Resolution of rate constants as closely similar as this is beyond the capability of our system. We therefore attribute the transient we observe to the decay of both enols and take the rate constant derived from this decay to be the average of values for the cis and trans isomers.


(13)

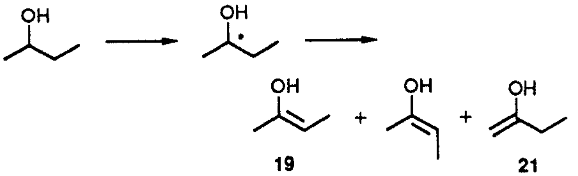

15


16


17


18

The ketyl radical derived from 2-butanol can also give cis and trans isomeric enols, and a regioisomer as well, eq 14. Here again we observed one less than the expected full number of transients, and we attribute this result once more to our inability to resolve rates of decay of the cis and trans isomeric enols. The two transients we did see, in addition to that assignable to the enol of the oxidant, differed in reactivity by an order of magnitude. Since a rate-retarding β-methyl group is present in the cis–trans pair and is absent in their regioisomer, we assigned the slower decay to the cis and trans pair, **19** and **20**, and the faster decay to their regioisomer, **21**.


(14)

19 **20** **21**

These ketonization reactions were examined in aqueous perchloric acid solutions. Rate measurements were made over a range of acid concentrations, usually encompassing variation by a factor of 10, at constant ionic strength (0.10 M). In all cases, observed first-order rate constants were accurately proportional to acid concentration, and least-squares analysis gave the hydronium ion catalytic coefficients listed in Table I.[6]

Keto–Enol Equilibrium Constants. The hydronium ion catalytic coefficients for the ketonization reaction, $k^{K}_{H^+}$, were combined with corresponding values for enolization, $k^{E}_{H^+}$, to obtain keto–enol equilibrium constants according to the relationship $K_E = k^{E}_{H^+}/k^{K}_{H^+}$. This provided K_E values for the enolization of ketones **1**–**5** and individual K_E values for formation of the regioisomeric enols of ketone **6** (see Tables II and III). There is a potential difficulty, however, in applying this method to cases where cis and trans isomeric enols might exist, as in two of the systems examined here, compounds **7** and **8**.

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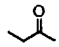
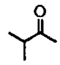
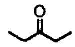
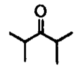
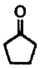
(17) Pruszynski, P.; Chiang, Y.; Kresge, A. J.; Schepp, N. P.; Walsh, P. A. *J. Phys. Chem.* **1986**, *90*, 3760–3766.

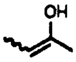
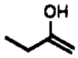
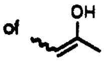
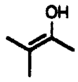
(18) Chiang, Y.; Kresge, A. J.; Wirz, J. *J. Am. Chem. Soc.* **1984**, *106*, 6392–6395. Keeffe, J. R.; Kresge, A. J.; Toullec, J. *Can. J. Chem.* **1986**, *64*, 1224–1227.

(19) Chiang, Y.; Chwang, W. K.; Kresge, A. J.; Yin, Y. *J. Am. Chem. Soc.* **1989**, *111*, 7185–7190.

(20) Chiang, Y.; Kresge, A. J.; Walsh, P. A.; Yin, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 869–871.

Table II. Comparison of Presently Determined Keto–Enol Equilibrium Constants with Literature Values[a]

ketone	pK_E							
	Schwarzenbach[b]	Gero[c]	Bell[d]	Dubois and Toullec[e]	thermochemical[f]	kinetic[g]	correlation[h]	present work
		2.92[i]			8.3[j]			7.50[i] 7.51[j]
							7.9[k]	7.33[k]
		3.17		7.7	7.8			7.43
		4.43		8.0			9.1	7.52
	4.32	3.06	4.89	8.0	7.2	6.7		7.94
	3.70	1.92	5.39	6.6	5.7	5.3		6.38
						6.8		8.00

[a] In aqueous solution at 25 °C unless specified otherwise. [b] Reference 21. [c] Reference 22; neat ketone, no solvent. [d] Reference 23. [e] Reference 24. [f] Reference 25. [g] Reference 26. [h] Reference 27. [i] pK_E for formation of both enols ( and ). [j] pK_E for formation of  only). [k] pK_E for formation of  only).

In such situations there are two separate enol-forming reactions, one giving the cis enol, eq 15, and another giving the trans, eq 16, and these are governed by two keto–enol equilibrium constants, K_E^c and K_E^t. An overall keto–enol equilibrium constant may also be defined in terms of the total enol concentration, as the sum of the concentrations of both enols divided by the concentration of the keto form, eq 17. This overall constant is equal to the sum of the individual cis and trans constants, which in turn may be expressed in terms of the individual enolization and ketonization rate constants, as shown in eq 18.

$$\text{keto} \overset{K_E^c}{\rightleftharpoons} \text{cis};\ K_E^c = [\text{cis}]/[\text{keto}] \qquad (15)$$

$$\text{keto} \overset{K_E^t}{\rightleftharpoons} \text{trans};\ K_E^t = [\text{trans}]/[\text{keto}] \qquad (16)$$

$$K_E = ([\text{cis}] + [\text{trans}])/[\text{keto}] \qquad (17)$$

$$K_E = K_E^c + K_E^t = (k_E^c/k_K^c) + (k_E^t/k_K^t) \qquad (18)$$

Such individual rate constants are not available from the present study, and observed values were therefore used instead, eq 19. These observed values are composites of the individual constants:

$$K_E^{obs} = k_E^{obs}/k_K^{obs} \qquad (19)$$

k_E^{obs} is the sum of the rate constants for formation of both enol isomers, eq 20, and k_K^{obs} is the average of the rate constants for ketonization of both enol isomers, eq 21. Substitution of these relationships into eq 19 leads to an expression, eq 22, which is equivalent to eq 18 only when $k_E^c/k_E^t = k_K^c/k_K^t$, i.e. when $K_E^c = K_E^t$ and the concentrations of the cis and trans isomers at equilibrium are equal.

$$k_E^{obs} = k_E^c + k_E^t \qquad (20)$$

$$k_K^{obs} = (k_K^c + k_K^t)/2 \qquad (21)$$

$$K_E^{obs} = 2(k_E^c + k_E^t)/(k_K^c + k_K^t) = k_E^{obs}/k_K^{obs} \qquad (22)$$

Fortunately, the difference between eqs 18 and 22 is small for the sort of deviations from equal concentrations of cis and trans isomers likely to be encountered in simple enol systems. A case in point is provided by phenylacetaldehyde and its enols where special circumstances have allowed determination of all of the individual rate constants.[20] The ratio of enol isomers at equilibrium in this system is [cis]/[trans] = 0.49, but K_E^{obs} calculated by eq 22 is only 10% less than that calculated by eq 18. It seems probable, therefore, that values of K_E^{obs} calculated from the present data are reasonably good approximations of K_E.

Comparison with Literature Values. A summary of pK_E values for those substrates examined here whose keto–enol equilibrium constants have been determined elsewhere is given in Table II. The first three sets of previous results, those due to Schwarzenbach,[21] Gero,[22] and Bell,[23] were performed by various refinements of the Meyer halogen titration method. It may be seen that all of these gave keto–enol equilibrium constants that were much too high, often by three or four orders of magnitude. This method relies upon the great lability of enols, but general inertness of ketones, toward reaction with halogens. The enol contents of the systems listed in Table II are very low, often only a few parts per billion, and halogen titration of substances present in such small amount is difficult.[28] This is reflected in the poor agreement with present results.

Dubois and Toullec also used the reaction of enols with halogen, but they measured rates rather than performing titrations. They performed their rate measurements at very low halogen concentrations, under conditions where the rate of reaction of enol with halogen, $k_2[X_2]$, is comparable to its rate of reversion to ketone, k_K, eq 23. In such a situation, the ratio of halogenation to ketonization rate constants, k_2/k_K, can be determined in addition to the specific rate of enolization, k_E, and an estimate of k_2 then allows evaluation of k_K and calculation of K_E as k_E/k_K.

$$\text{ketone} \underset{k_K}{\overset{k_E}{\rightleftharpoons}} \text{enol} \xrightarrow[k_2]{X_2} \qquad (23)$$

Dubois and Toullec believed that the halogenation step was a diffusion-controlled process, and they assigned the value $k_2 = 5 \times 10^9$ M^{-1} s^{-1} to its rate constant. The results they obtained in this way are in reasonably good agreement with the presently determined values, often within the ±0.3 pK unit uncertainty

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(21) Schwarzenbach, G.; Wittwer, C. Helv. Chim. Acta 1947, 30, 669–674.

(22) Gero, A. J. Org. Chem. 1954, 19, 1960–1970.

(23) Bell, R. P.; Smith, P. W. J. Chem. Soc. 1966, 241–243.

(24) Dubois, J. E.; El-Alaoui, M.; Toullec, J. J. Am. Chem. Soc. 1981, 103, 5393–5401.

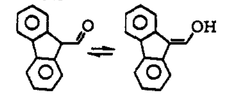
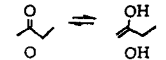
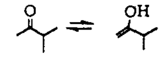
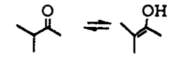
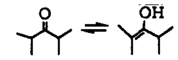
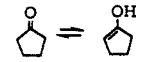
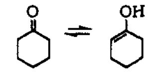
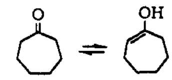
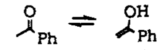
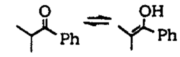
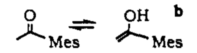
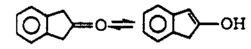
(25) Guthrie, J. P.; Cullimore, P. A. Can. J. Chem. 1978, 57, 240–248.

(26) Guthrie, J. P. Can. J. Chem. 1978, 57, 797–802.

(27) Guthrie, J. P. Can. J. Chem. 1978, 57, 1177–1185.

(28) Allinger, N. L.; Chow, L. W.; Ford, R. A. J. Org. Chem. 1967, 32, 1994–1995.

Table III. Summary of Keto-Enol Equilibrium Constants[a]

system	pK_E	ref
	6.23	7
	3.86	16a
	3.35	20
	3.07	20
	0.98	30
	-1.23	31
	8.33	32
	8.76	this work
	8.61	this work
	8.76	this work
	7.51	this work
	7.33	this work
	7.43	this work
	7.52	this work
	7.94	this work
	6.38	this work
	8.00	this work
	7.96	18
	6.48	17
 b	6.92	33
	3.84	34

[a] In aqueous solution at 25 °C. [b] Mes = mesityl (2,4,6-trimethylphenyl).

claimed by Dubois and Toullec for their method, despite the fact that the halogenation step is now known to be not quite, though almost, diffusion-controlled.[15] Toullec later provided revised values of pK_E using instead of $k_2 = 5 \times 10^9$ M^{-1} s^{-1} a number recently determined for the enol of acetophenone, $k_2 = 2.9 \times 10^9$ M^{-1} s^{-1}.[11] These pK_E's,[29] all less than the values listed in Table II by the constant amount 0.24, are in still better agreement with the present results even though it is now known also that k_2 varies somewhat with enol structure[15] and a constant value should consequently not be used in such a calculation.

Guthrie's results are also in reasonable agreement with the presently determined values, again often within the somewhat greater, ±1.0 pK unit, uncertainty claimed for each of his methods. Guthrie's methods require assumptions as well. The thermochemical method uses a linear free energy relationship, based upon estimated enol pK_a's, to provide free energies of formation of the enols, which it then combines with known free energies of formation of the keto isomers to calculate K_E.[25] The kinetic method[26] uses the relationship $K_E = k_E/k_K$, with rate constants for hydrolysis of methyl vinyl ethers substituted for k_K, and the correlation method[27] deduces K_E values from a Marcus theory relationship. The general agreement between the results obtained by these methods and our directly measured values shows that the assumptions made are not unreasonable.

Discussion

A summary of the keto-enol equilibrium constants determined here, plus some other values with which it is instructive to compare the present results, is presented in Table III. It may be seen that the enol content of ketones is generally smaller than that of corresponding aldehydes, e.g. $pK_E = 8.33$ for acetone versus $pK_E = 6.23$ for acetaldehyde, and $pK_E = 7.33$ for methyl isobutyl ketone versus $pK_E = 3.86$ for isobutyraldehyde. This difference may be attributed to stabilization of the keto isomer by electron donation to its positively charged carbonyl carbon atom; ketones have two alkyl groups to provide such stabilization whereas aldehydes have only one.

The effect appears to be general, and of much the same magnitude, for all simple alkyl groups: the keto-enol equilibrium constants for enolization into the methyl group of methyl ethyl ketone, $pK_E = 8.76$, methyl isopropyl ketone, $pK_E = 8.61$, and methyl *tert*-butyl ketone, $pK_E = 8.76$, are not very different from one another, and they are also very close to the symmetry corrected value for acetone, $pK_E = 8.63$. A phenyl substituent in this position also lowers the enol content, but to a somewhat lesser extent than do alkyl groups: $pK_E = 7.96$ for acetophenone.[18]

Alkyl and phenyl groups, of course, also stabilize carbon-carbon double bonds,[35] and they should therefore affect the enol isomer as well. This effect is evidently overwhelmed by that on the keto isomer when the substituent is in the α-position, but it becomes dominant when substitution takes place at the other end of the double bond, in the β-position. For example, $pK_E = 3.86$ for isobutyraldehyde versus $pK_E = 6.23$ for acetaldehyde and $pK_E = 6.48$ for isobutyrophenone versus $pK_E = 7.96$ for acetophenone. Similarly, 2-butanone and 3-methyl-2-butanone enolize preferentially to the enol isomers having the more highly alkylated double bond; the favored isomer is more stable in these cases by ca. 1.7 kcal/mol. A phenyl substituent in the β-position has a somewhat stronger effect, consistent with its weaker influence when placed in the α-position: $pK_E = 3.35$ and 3.07 for phenylacetaldehyde in equilibrium with its cis and trans enols, respectively, versus $pK_E = 6.23$ for acetaldehyde. Two phenyls are better than one, as evidenced by $pK_E = 0.98$ for diphenylacetaldehyde. When coplanarity with the carbon-carbon double bond of the enol is forced upon the phenyl groups, as in the fluorenylacetaldehyde system, $pK_E = -1.23$, the effect becomes even stronger, enough so to make enol the more stable isomer. The effect of improved coplanarity may also be seen in the comparison of 2-indanone, $pK_E = 3.84$, with acetone, $pK_E = 8.33$; the effect of a single phenyl group here is greater than that in going from acetaldehyde to phenylacetaldehyde.

Keto-enol equilibria in the cyclic 5-, 6-, and 7-membered-ring systems show an interesting ring-size effect. The enol contents of cyclopentanone and cycloheptanone are low and comparable to those of open chain analogues, whereas the enol content of cyclohexanone is nearly two orders of magnitude greater. This greater enol content of cyclohexanone over that of cyclopentanone agrees with an estimate made on the basis of calorimetric measurements,[36] and it is consistent with the known tendency of endocyclic double bonds, such as those in the enol isomers of these systems, to be less stable in 5-membered rings than in 6-membered

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(29) Toullec, J. *Tetrahedron Lett.* **1984**, *39*, 4401-4402.

(30) Chiang, Y.; Kresge, A. J.; Krogh, E. T. *J. Am. Chem. Soc.* **1988**, *110*, 2600-2607.

(31) Harcourt, M. P.; More O'Ferrall, R. A. *Bull. Soc. Chim. Fr.* **1988**, 407-414.

(32) Chiang, Y.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1989**, *111*, 3977-3980.

(33) Kresge, A. J.; Schepp, N. P. *J. Chem. Soc., Chem. Commun.* **1989**, 1548-1549.

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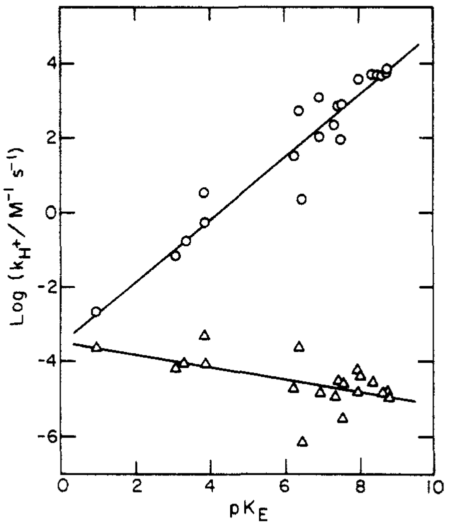

Figure 5. Relationship between hydronium ion catalytic coefficients for enolization (△) and ketonization (○) and pK_E for simple aldehydes and ketones in aqueous solution at 25 °C.

rings.[37] The origin of the alternation in enol content in going from the 5- to the 6- to the 7-membered-ring system is less clear. A similar alternation has been found in the keto–enol equilibrium of α-carbomethoxycycloalkanones,[38] and also in the exo–endo double bond isomerization of isopropylidenecycloalkanes to 1-isopropylcycloalkenes,[39] but not in the similar isomerization of methylenecycloalkanes to 1-methylcycloalkenes, for which $K_{endo/exo}$ decreases regularly from 5- to 6- to 7-membered-ring systems.[40]

This alternating ring-size effect appears also in both of the rate constants that make up K_E. The data of Table I show that rates of enolization of the cyclic ketones fall in the order 6 > 5 ≈ 7 and that there is a converse relationship, 5 ≈ 7 > 6, for rates of ketonization. The reactivity order 6 > 5 ≈ 7 has also been observed for enolization in a different solvent,[41] and the ketonization order 5 ≈ 7 > 6 is similar to that found for hydrolysis of the corresponding ethyl vinyl ethers.[42]

The converse nature of the reactivity orders shown by enolization and ketonization in these systems indicates that structural effects on the keto–enol equilibria are expressed in a complementary fashion in the forward and reverse reactions. Such sharing of structural effects extends to the other keto–enol systems of Table III. Figure 5 shows that both the enolization rate constants and the ketonization rate constants correlate in these systems with the equilibrium constants; the slopes of the two correlations, moreover, are of opposite sign, indicating that the relationships are converse.[43]

The forward and reverse reactions, however, do not share the structural effects equally. Ketonization is considerably more sensitive to structural changes than is enolization, as shown by the greater absolute magnitude of its correlation slope, 0.83 ± 0.06, in comparison to that for enolization, 0.17 ± 0.06.

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Registry No. 1, 464-07-3; **2**, 600-36-2; **3**, 96-41-3; **4**, 108-93-0; **5**, 502-41-0; **6**, 598-75-4; **7**, 584-02-1; **8**, 78-92-2; **9**, 79144-27-7; **10**, 34454-78-9; **12**, 557-75-5; **21**, 61923-55-5; MeC(O)CH_2Me, 78-93-3; MeC(O)$CHMe_2$, 563-80-4; Me_3CC(O)Me, 75-97-8; MeCH_2C(O)CH_2Me, 96-22-0; Me_2CHC(O)$CHMe_2$, 565-80-0; H_2C=C(OH)CMe_3, 79144-28-8; MeCH=C(OH)Me, 21411-38-1; MeCH=C(OH)CH_2Me, 38553-82-1; Me_2C=C(OH)$CHMe_2$, 113249-34-6; *i*-PrOH, 67-63-0; Me_2CO, 67-64-1; MeC(OH)=CH_2, 29456-04-0; D_2, 7782-39-0; MeCHO, 75-07-0; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; cycloheptanone, 502-42-1; cyclopenten-1-ol, 59557-02-7; cyclohexen-1-ol, 4065-81-0; cyclohepten-1-ol, 116725-78-1.

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[43] Fluorenyl carboxaldehyde was omitted from these correlations because hydronium ion catalytic coefficients are not available for this system.

Observation of a Remarkable Dependence of the Rate of Singlet–Singlet Energy Transfer on the Configuration of the Hydrocarbon Bridge in Bichromophoric Systems

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Abstract: Intramolecular singlet energy transfer can be detected in a series of rigid bichromophoric molecules (**1**(*n*)) where a dimethoxynaphthalene chromophore and a carbonyl chromophore are separated by extended all-trans arrays of up to eight C–C σ bonds (**1**(**8**)). In the series of compounds **2**(*n*) "kinks" are introduced in the array of σ bonds of the saturated hydrocarbon system, which bridges the chromophores. Singlet energy transfer is then much less efficient (i.e. in **2**(**6**)) or even absent (i.e. in **2**(**8**)), which supports the earlier interpretation of the energy transfer mechanism in **1**(*n*) as being mainly mediated by through-bond exchange interaction and furthermore explains the virtual absence of such interaction in more flexible systems where the chromophores are linked by polymethylene bridges.

Transfer of electronic energy between chromophores, located in different molecular entities or covalently connected to a single (macro)molecular framework, plays a vital role in many photophysical and photochemical processes, including such widely

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