Conformational Flexibility and Photochemistry

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Rates at which electronically excited states react chemically are often as fast as rates at which they undergo conformational change. The competition between these quite different processes produces several intriguing effects that are not possible in ground-state chemistry. This competition can be considered from different viewpoints. One can ask how lack of conformational mobility might limit the photoreactions available to certain classes of compounds. Such limitations may be "good" if they prevent unwanted reactions or "bad" if they prevent a desired reaction. Recent synthetic applications of intramolecular photocyclizations[1,2] have recognized this point. Alternatively, photochemical reactions can be studied to monitor rates of conformational change.[3] In particular, excited-state behavior in systems subject to conformational restraints can provide unique information about the orientational requirements for the interaction of two functional groups.

This Account will examine intramolecular *bifunctional* photoreactions of organic molecules, wherein two distinct functional groups separated by a carbon skeleton react only after one of them is electronically excited and the other is close enough for the two to interact. Such interactions have been studied extensively by spectroscopic methods.[3] The emphasis here will be on *chemical* transformations so as to highlight the interplay between photochemical reaction efficiency and conformational flexibility.
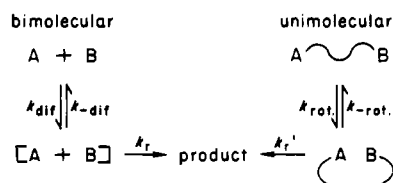
Inter- vs. Intramolecular Bifunctional Reactions

Most intermolecular reactions, which necessarily involve two distinct functionl groups, can have intramolecular counterparts. That there should be analogies between the kinetics of bimolecular and unimolecular bifunctional reactions has, in fact, been considered in recent reviews for both excited-state[3] and ground-state[4] reactions.

Scheme I shows the parallel between diffusion together of two molecules and rotation together of two functional groups in the same molecule. Two kinetic extremes develop in each case, corresponding to reaction of the two moieties A and B being either much slower or much faster than their movement apart.

Observed rate constants for "slow" reactions represent a "real" structure-dependent rate constant k_r modified

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Scheme I
Kinetics of Bifunctional Reactions

Scheme II
The Photosensitive Bichromophoric Bug
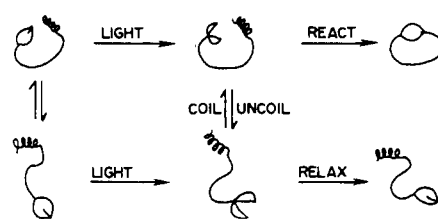
by a preequilibrium constant. The major difference between inter- and intramolecular reactions is that conformational equilibrium constants K_{rot}, are much more sensitive to structure[3-5] than are K_{dif} values.

Diffusion-controlled bimolecular reactions, especially of reactive intermediates, are a well-known phenomenon. Rotation-controlled reactions represent the intramolecular equivalent and should be expected whenever the bimolecular reaction between A and B is known to be diffusion controlled. A rotation-controlled reaction of a stable molecule is a contradiction in terms, since the compound would react as soon as it was made. Therefore the phenomenon is restricted to highly energetic molecules, such as those formed by absorption of light.
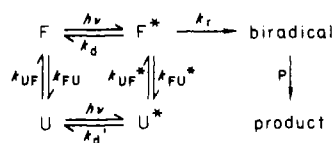
For a zoomorphic description of the title situation, imagine a bug that opens its mouth when struck by light, can hold it open for only a short time, and during that time can swallow anything within striking range of its open mouth including its own tail.[6] Scheme II depicts this creature and the dynamics of its externally provoked self-mutilation.

The bug represents a conformationally mobile excited state. Its relative hunger and agility define three dis-

(1) For example, see: (a) Wender, P. A.; Howbert, J. J. *J. Am. Chem. Soc.* 1981, *103*, 688. (b) Oppolzer, W. *Acc. Chem. Res.* 1982, *15*, 135.
(2) Paquette, L. A.; Balogh, D. W. *J. Am. Chem. Soc.* 1982, *104*, 774. Ternansky, R. J.; Balogh, D. W.; Paquette, L. A. *Ibid.* 1982, *104*, 4503.
(3) Winnik, M. A. *Chem. Rev.* 1981, *81*, 491.
(4) Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* 1981, *14*, 95.
(5) Winstein, S.; Holness, N. J. *J. Am. Chem. Soc.* 1955, *77*, 5562.
(6) The author is proud to be able to trace his educational geneology directly to Kekulé.

Scheme III
Competition between Triplet Reaction and Bond Rotation

$$F \underset{k_d}{\overset{h\nu}{\rightleftharpoons}} F^* \xrightarrow{k_r} \text{biradical}$$

$$k_{UF} \Big\Vert k_{FU} \quad k_{UF}^* \Big\Vert k_{FU}^* \qquad P \Big\vert$$

$$U \underset{k_{d'}}{\overset{h\nu}{\rightleftharpoons}} U^* \qquad \text{product}$$

conformational equilibrium: $k_{FU}^*, k_{UF}^* \gg k_r, k_d$

$$k_{obsd} = k_r k_{UF}^* / (k_{FU}^* + k_{UF}^*) = x_F^* k_r$$

$$\Phi = \frac{k_r x_F^* P}{k_r x_F^* + k_d x_F^* + k_{d'} x_U^*}$$

ground-state control: $k_{FU}^*, k_{UF}^* \ll k_r, k_d$

$$k_{obsd}(F) = k_r$$

$$\Phi = k_R x_F P / (k_R + k_d)$$

rotational control: $k_{UF}^* \sim k_d : k_{FU}^* \ll k_r$

$$k_{obsd}(F) = k_r \qquad k_{obsd}(U) = k_{UF}^*$$

$$\Phi = \frac{k_R x_F P}{k_R + k_d} + \frac{k_{UF} x_U^* P}{k_{UF}^* + k_{d'}}$$

crete situations. A vigorous young bug, thrashing about rapidly, may be either starved or relatively sated. In the latter case, it coils and uncoils many times before finally biting its tail (reacting) or closing its mouth (relaxing). In the former case, it swallows its tail as soon as it finds it. An arthritic old bug, however, may suffer such impaired mobility that it cannot keep its mouth open long enough to find its tail at all. Only if this tired bug is in the proper coiled conformation when struck by light can it bite its tail.

Scheme II can be removed to the abstract as in Scheme III, where F and U represent conformations that are favorable and unfavorable, respectively, for a given intramolecular interaction. Three separate limiting situations arise, depending on how rates of excited-state conformational change compete with chemical and physical decay rates of the excited state.

With relatively slow excited-state reactions, conformational equilibrium is established before reaction. Observed rate constants include excited-state conformational equilibrium constants. There is only one kinetically distinct excited state even if two different conformations undergo two different reactions.

With fast excited-state reactions and/or slow conformational change, the quantum efficiency for the intramolecular reaction of interest is limited by the ground-state population of favorable conformations. There are at least two kinetically distinct excited states, only one of which (F*) leads to the reaction of interest. This situation is called "ground state control"[7] and applies only to reactions induced by instantaneous insertion of energy. Its bimolecular counterpart is called "static quenching".

Finally, if conformational change and decay are competitive, rotation-controlled reactions can occur. There again are two kinetically distinct excited states; the reaction of interest arises from both but determines the

lifetime of only one. The rate of conformational change is lifetime determining for the other. Note that partial ground-state control necessarily accompanies any rotationally controlled process. Whether or not the "static" component can be measured depends critically on what fraction of ground-state molecules exist in conformation F.

Examples of Various Boundary Conditions in Ketone Photochemistry

This Account will consider conformationally sensitive ketone photoreactions. The choice is not arbitrary, since ketones are the only compounds whose photochemistry has been so fully studied and which occur in such structural variety that examples of all three kinetic extremes have been firmly established.

Excited ketones undergo only three common bifunctional reactions: hydrogen atom abstraction, electron transfer, and electronic energy transfer.[8] Each of these processes can occur internally in suitable bifunctional molecules. All three processes occur from both excited singlets and triplets. The latter are more important as regards competition with conformational motion because of the rapid intersystem crossing rates in ketones.[9]

Of these three reactions, hydrogen abstraction is the best understood geometrically: the carbonyl oxygen must approach within bonding distance of a labile H atom. Since the other two processes do not involve any bonding–rebonding, thay can occur over variable distances.

Rate constants for bimolecular hydrogen atom abstraction by triplet ketones are much smaller than those for diffusion controlled reactions.[10] Consequently, conformationally flexible ketones are expected to attain conformational equilibrium before their excited states undergo intramolecular reaction. However, cyclic ketones may suffer sufficiently impaired rotational freedom that their excited-state reactions are subject to ground-state control or rotational control.

Conformational Equilibrium Before γ-Hydrogen Abstraction

Triplet ketones obey the general rule that, in flexible acyclic systems, 1,5 hydrogen atom transfers are the most rapid.[11] For example, γ-hydrogen abstraction (which leads to Norrish type II reactions[12]) is some 20 times faster than the equivalent δ-hydrogen abstraction in acyclic ketones.[13] The seven-atom cyclic transition state for the latter process is disfavored both statistically and energetically. This preference for γ-hydrogen abstraction is an example of the Curtin-Hammett principle,[14] the molecule being flexible enough to freely choose among transition states of various shapes and energies, with the six-membered cyclic transition state being uniquely able to achieve a strainfree chairlike geometry.[13]

(7) The term "ground state control" was originally coined to describe how molecular conformations can affect the competing photoreactions of single, extended functional groups such as in polyenes; for example, see: (a) Dauben, W. G.; Kellogg, N. S. *J. Am. Chem. Soc.* **1980**, *102*, 4456. (b) Baldwin, J. E.; Krueger, S. M. *Ibid.* **1969**, *91*, 6444; and references in each.

(8) Wagner, P. J. *Top. Curr. Chem.* **1976**, *66*, 1–52.
(9) Lower, S. K.; El-Sayed, M. A. *Chem. Rev.* **1966**, *66*, 199.
(10) (a) Scaiano, J. C. *J. Photochem.* **1973/1974**, *2*, 168. (b) Giering, L.; Berger, M.; Steel, C. *J. Am. Chem. Soc.* **1974**, *96*, 953.
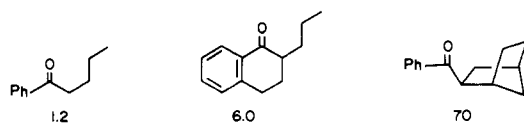(11) Hesse, R. H. *Adv. Free Rad. Chem.* **1969**, *1*, 83.
(12) Wagner, P. J.; *Acc. Chem. Res.* **1971**, *4*, 168.
(13) Wagner, P. J.; Kelso, P. A.; Kemppainen; A. E.; Zepp, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 7500.
(14) Eliel, E. L. "Stereochemistry of Carbon Compounds", McGraw-Hill: New York, 1962; pp. 151, 237.

Scheme IV
k_H (10^8 s^{-1}) as a Function of Molecular Rigidity

The observed rate constant for a given γ-hydrogen abstraction contains the factor χ_F, which describes the equilibrium fractional population of favorable conformations, ones from which γ-hydrogen abstraction can take place with the intrinsic rate constant k°. (To be

$$k_{obsd} = \chi_F k^\circ \qquad (1)$$

completely exact, eq 1 should sum over all favorable conformations, each with its own k°.[8]) In general, χ_F factors may differ between ground and excited states, inasmuch as electronic excitation changes bond angles and lengths. Since, n,π* excitation of carbonyls produces only a slight C–O bond lengthening, one can often assume correctly that χ_F* and χ_F(gs) do not differ significantly and use simply χ_F.

In cyclic ketones, the number of different conformations possible can get quite small, so that the value of χ_F can approach 1 or 0. An early example of χ_F being 0 was provided by 2-n-propylcyclohexanones.[15] The isomer with the propyl group held axial and thus too far from the carbonyl oxygen for O–H bonding undergoes no intramolecular hydrogen abstraction. This observation originally was offered as evidence for a stereoelectronic effect requiring approach of the C–H bond in the plane of the carbonyl oxygen's n orbital, perpendicular to the π orbital. It is now clear that any such requirement is not very rigid.[13,16]
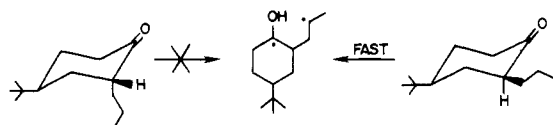
The rate constants for triplet-state γ-hydrogen abstraction listed in Scheme IV[17] nicely illustrate the rate enhancements produced as χ_F gets closer to 1. In all cases, the C–H bond being attacked is secondary, so that the measured rate variations must reflect primarily conformational effects. As the number of freely rotating C–C bonds between the carbonyl and the γ C–H is reduced, the rate constant increases. Each "frozen" rotation increases k_{obsd} and thus χ_F by an order of magnitude.

The rapid ring-puckering motions of most cycloalkanes allow conformational equilibrium to be established before excited-state decay.[18,19] For example, benzoylcyclobutanes undergo type II reactions in low quantum efficiency and display very long triplet lifetimes.[20] This situation was originally ascribed to a very low equilibrium population of the pseudoaxial conformer, with the pseudoequatorial conformer having no

Chart I
δ-H Abstraction from o-Alkoxy Ketones

| Φ | 0.20 | 0.30 | 0.95 | 0.78 |
| k_H | 0.02 | 0.13 | 1.8 | 20×10^7 |

accessible γ hydrogens. Triplet exo-5-benzoylbicyclo-[2.1.1]hexane, an appropriate model for the reactive conformer of benzoylcyclobutane, reacts with a rate constant of 5×10^9 s^{-1},[21] as expected for a molecule fixed into a favorable conformation.
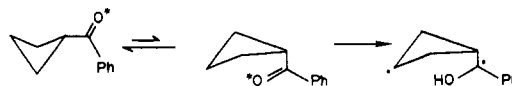
Alexander and Uliana[18] clarified the situation by studying several benzoylcyclobutanes with ring substituents known to change triplet reactivity.[22] They found a linear relationship between quantum yield and intrinsic triplet reactivity. This result eliminates the possibility of ground-state control, in which case quantum yields would have been independent of k_H (Scheme III). With k_H known (from the bicyclic model), analysis of the observed kinetics according to eq 1 yields a value for χ_F* close to 10^{-5}. Thus study of this photoreaction has provided a measure of a conformational equilibrium constant too small to determine by more classic techniques.

Remote Hydrogen Abstractions

Efficient intramolecular hydrogen abstractions occur from positions other than γ when there are no γ hydrogens or when conformational rigidity prevents access to γ hydrogens. The latter situation has not received much study but was exploited spectacularly by Paquette in his synthesis of dodecahedrane.[2] Several examples of the former situation follow.

Winnik has been studying remote hydrogen abstractions in order to assess chain coiling probabilities as a function of ring size.[23] In a series of n-alkyl esters of 4-benzoylbenzoic acid, the rate constant for remote H abstraction is negligible when $n < 9$ but increases by some 0.5×10^4 s^{-1} for each extra CH$_2$ group in the ester. These rate constants reflect the increased probability for cyclic conformations as carbon chains get longer. When $n = 20$, $k_{obsd} = 4.6 \times 10^4$ s^{-1}, with reactivity evenly distributed at each carbon between C-10 and C-19.[24] These results indicate that any one coil size in the range $n = 9–18$ is only $\sim 10^{-4}$ as probable as the six-membered ring that leads to γ-hydrogen abstraction.

We have recently measured conformational equilibrium constants that affect two different examples of δ-hydrogen abstraction.[25] Irradiation of o-alkoxyphenyl

(15) Turro, N. J.; Weiss, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 2185.
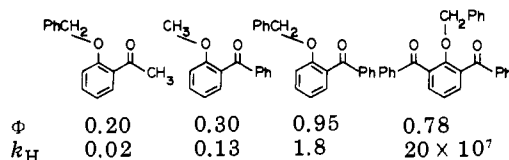(16) Lewis, F. D.; Johnson, R. W.; Ruden, R. A. *J. Am. Chem. Soc.* **1972**, *94*, 4292.
(17) Lewis, F. D.; Johnson, R. W.; Kory, D. R. *J. Am. Chem. Soc.* **1974**, *96*, 6100.
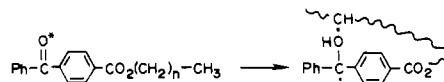(18) Alexander, E. C.; Uliana, J. A. *J. Am. Chem. Soc.* **1974**, *96*, 5644.
(19) Lewis, F. D.; Johnson, R. W.; Johnson, D. E. *J. Am. Chem. Soc.* **1974**, *96*, 6090.
(20) Padwa, A.; Alexander, E.; Niemcyzk, M. *J. Am. Chem. Soc.* **1969**, *91*, 465.
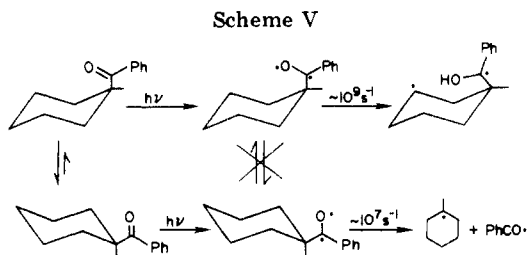
(21) Padwa, A.; Eisenberg, W. *J. Am. Chem. Soc.* **1972**, *94*, 5859.
(22) Wagner, P. J.; Kemppainen, A. E.; Scott, H. N. *J. Am. Chem. Soc.* **1973**, *95*, 5604.
(23) Winnik, M. A.; Lee, C. K.; Basu, S.; Saunders, D. S. *J. Am. Chem. Soc.* **1974**, *96*, 6182. Winnick, M. A. *Acc. Chem. Res.* **1977**, *10*, 173.
(24) Breslow, R.; Rothbard, J.; Herman, F.; Rodriguez, M. L. *J. Am. Chem. Soc.* **1978**, *100*, 1213.
(25) Meador, M. A.; Wagner, P. J. *J. Am. Chem. Soc.* **1983**, *105*, 4484; manuscript in preparation.

Scheme V

ketones is known to produce dihydrobenzofuranols, presumably by cyclization of 1,5-diradicals.[26] Chart I compares the behavior of several such ketones. The measured triplet lifetimes and high quantum yields indicate that k_{obsd} for δ-hydrogen abstraction is proportional to the intrinsic k_H values, the methoxybenzophenone being less reactive than the (benzyloxy)benzophenone and the acetophenone (with a π,π^* lowest triplet) being even less reactive. Therefore the triplet states achieve dynamic conformational equilibrium before decaying. In the dibenzoyl ether, there is a carbonyl group near the benzyl C–H bonds no matter which way the alkoxy group is twisted. The 10-fold rate enhancement afforded by the extra benzoyl group suggests an equilibrium constant of 10 for rotation of the alkoxy group about the phenyl–O bond, with the unreactive anti rotamer favored in the monoketones.
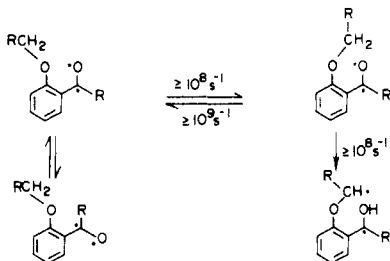
We also find that α-(o-alkylphenyl) ketones undergo photocyclization to 2-indanols via triplet-state δ-hydrogen abstraction.[25] Rate constants are proportional to intrinsic k_H values (o-cumyl 6 times more reactive than o-tolyl). The α-mesityl ketone is 8 times more reactive than the α-o-tolyl. This rate enhancement afforded by a second o-alkyl group indicates a syn–anti rotational equilibrium constant on the order of 3 in favor of the unreactive conformer in the α-o-tolyl ketone.
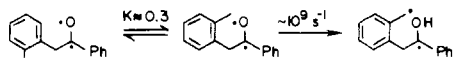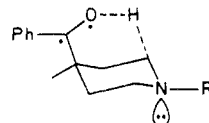

Ground-State Control of Hydrogen Abstraction

Several benzoylcyclohexane derivatives have provided the most clear-cut examples of ground-state control in any photoreaction. Lewis reported that α cleavage and γ-hydrogen abstraction are competing triplet reactions in 1-benzoyl-1-methylcyclohexane just as in the corresponding cyclopentane derivative.[19] However, in the cyclohexane the two processes occur from kinetically distinct triplets. The two different products are quenched with distinctly different efficiencies. The measured rate constant for α-cleavage is 2×10^7 s^{-1} and that for γ-hydrogen abstraction is 6×10^8 s^{-1}. The two triplet reactions both proceed much faster than the

$\sim 10^5$ s^{-1} ring inversion of cyclohexane. The conformer with benzoyl axial can undergo internal hydrogen abstraction rapidly; its epimer cannot and therefore undergoes the slower α cleavage. Some 75% of the ground-state molecules have a benzoyl group equatorial. Upon excitation, that 75% cleave into radicals before any ring inversion can occur.

We later observed the same phenomenon in 4-benzoyl-4-methylpiperidines.[27] The axial/equatorial ratio in the piperidines is comparable to that in the corresponding cyclohexane, and product ratios are completely controlled by equilibrium ground-state conformational populations. One unusual aspect of this reaction is its quencher-controlled selectivity. In the presence of sufficient triplet quencher, the only product is that corresponding to type II cyclization. Since cyclic alcohol formation is barely quenchable, the readily quenchable cleavage reaction can be totally suppressed so that only the conformer with axial benzoyl reacts. Hydrogen abstraction by this conformer is much faster ($\sim 10^{10}$ s^{-1}) than in the corresponding cyclohexane. This rate enhancement reflects a nice stereoelectronic effect, the lone pair on the nitrogen being held perfectly trans periplanar to the axial γ C–H bonds.

Rotationally Controlled Hydrogen Abstraction

There are several reports of intramolecular bifunctional quenching processes proceeding with rate constants so large that they must correspond to conformational change. The clearest example of rotation control in a photochemical reaction is provided by the photoenolization of o-alkylphenyl ketones.[28-31] This basic photochromic system remained mechanistically confusing until it was realized that two kinetically and conformationally distinct triplets are involved.[28] Sensitization studies[32] revealed that ketones such as o-methylacetophenone and o-methylbenzophenone produces two distinct triplets, one with a subnanosecond lifetime and another with a ~ 30 ns lifetime (in benzene). Recent flash kinetic work has verified these conclusions.[31] That these different triplets correspond to syn and anti conformers was indicated by the behavior of 8-methyl-1-tetralone, which is locked into a syn conformation and which displays only a nanosecond triplet.[28]
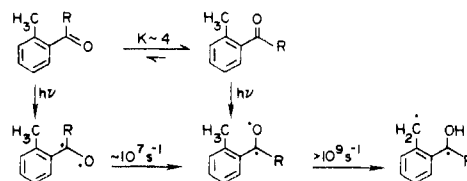
Enolization of the syn triplet corresponds to γ-hydrogen abstraction from a geometrically perfect con-

(26) (a) Lappin, G. R.; Zannucci, S. *J. Org. Chem.* 1971, *36*, 1808. (b) Pappas, S. P.; Zehr, R. D. *J. Am. Chem. Soc.* 1971, *93*, 7112. (c) O'Connell, E. J. *Ibid.* 1968, *90*, 6550.

(27) Wagner, P. J.; Scheve, B. J. *J. Am. Chem. Soc.* 1977, *99*, 1858.
(28) Wagner, P. J.; Chen, C.-P. *J. Am. Chem. Soc.* 1976, *98*, 239.
(29) Haag, R.; Wirz, J.; Wagner, P. J. *Helv. Chim. Acta* 1977, *60*, 2595.
(30) Wagner, P. J. *Pure Appl. Chem.* 1977, *49*, 259.
(31) Das, P. K.; Encinas, M. V.; Small, R. D.; Scaiano, J. C. *J. Am. Chem. Soc.* 1979, *101*, 6965.
(32) Wagner, P. J. *J. Photochem.* 1979, *10*, 387.

formation, with $\chi_F \approx 1$. Its rapidity is in accord with the considerations presented above. That the decay of the longer lived triplet corresonds to anti → syn rotation was deduced from the structure independence of the rate constant. Thus valerophenones with o-CH_3, CD_3, and CH_2CH_3 groups all undergo competitive type II elimination and enolization, the latter occurring at the same rate in all three. The rate-determining step obviously does not involve H-atom abstraction. (Note the contrasting behavior of the o-alkoxy ketones discussed above). Stern–Volmer quenching studies indicate that enolization of several o-methyl ketones occurs from both long-lived and short-lived triplets.[30] Therefore, since the longer-lived triplets undergo hydrogen transfer but not in the rate-determining step, the rate-determining step for enolization is deduced to be bond rotation.

It is worth emphasizing that the bond rotation rate constant of 2–3×10^7 s^{-1} deduced from these studies is slower than in the ground state because of the additional conjugation between phenyl ring and carbonyl group found in the excited state.

Since these o-alkyl ketones are subject to ground-state control, the fraction of the absorbed light that produces the longer lived triplet represents an otherwise inaccessible measure of the ground-state equilibration between syn and anti conformers. Sensitization and flash studies both indicate that 10–35% of the absorbed light produces the longer lived anti triplet, the exact fraction depending on structure. The larger the o-alkyl group and the more substituted the α carbon, the smaller the fraction of anti rotamer,[32] as would be expected from the increased steric interactions.

Intramolecular Orbital Interactions

A wide variety of intramolecular electron-transfer processes have been studied, some for the express purpose of deducing orientational requirements for such processes.[33] Nonetheless, no clear picture has emerged of the relative orientational requirements of donor and acceptor. Many of the systems studied have involved donors and acceptors with extended π systems; in such cases sufficient orbital overlap for rapid reaction apparently is possible over a large range of orientations and distances. Therefore we have purposely studied some n-orbital systems where overlap is more limited.

Photochemistry of $PhCO(CH_2)_nX$

Several laboratories have looked at intramolecular interactions in α-substituted ω-benzoylalkanes. These systems most resemble the light-sensitive bug of the Introduction. Table I summarizes the results for X = thioalkoxy,[34] dimethylamino,[35] and vinyl.[36] The primary interest in such studies is how the rate constant for internal quenching of triplet ketone varies with n and with the nature of X.

The RS and R_2N groups provide the most informative results precisely for the reason that they were studied. Both sulfides and tertiary amines quench triplet ketones by charge-transfer interactions.[37,38] The

Table I
Rate Constants (10^7 s^{-1}) for Internal Quenching in Triplet $PhCO(CH_2)_nX^a$

n/X	SBu	NMe_2	$CH=CH_2$
1	130	<10	
2	460	430	80
3	240	740	<10
4	14	50	
5	<2	20	
k_2^b	30	300	0.8

^{a} In benzene at 25 °C. ^{b} Analogous bimolecular rate constant.

amines display 10-fold larger bimolecular quenching rate constants because of their lower oxidation potentials. The simplest picture of such charge-transfer quenching involves the formation of an exciplex with significant overlap of the donor HOMO with the acceptor LUMO.[39–42] In these particular cases, both orbitals are highly directed and highly localized n orbitals: the lone pair on S or N as donor, the half-vacant carbonyl n orbital in the n,π* benzoyl triplet as acceptor. Since such overlap resembles σ-bond formation, the molecular must attain a conformation something like that of a cycloalkane for CT quenching to occur. How exact the resemblance is will depend on how closely the donor and acceptor orbitals must approach each other.

The number of atoms in these cyclic interactions equals $n + 3$. Therefore it is significant that both donors display the fastest quenching when $n = 2$ or 3, reflecting the expected ease of formation of five- and six-membered rings. As n gets larger, k decreases dramatically, reflecting the expected decreased probability of forming medium-sized rings. In both cases, k is also lower when $n = 2$, as expected for four-membered ring formation, but there is no disappearance of reactivity as for β-hydrogen abstraction. It is interesting that the $n = 3/n = 4$ rate ratios are the same as that for γ/δ hydrogen abstraction. The similarity suggests that entropic effects dominate for both processes when $n > 3$.

The difference in the intrinsic quenching abilities of RS and R_2N is important. The bimolecular reaction between triplet ketones and dialkyl sulfides is substantially slower than diffusion-controlled reactions. Given the rapidity of bond rotations in acyclic systems, the intramolecular kinetics should display conformational control. Bimolecular quenching by tertiary amines is partially diffusion controlled. In this case one might expect some rotational control and perhaps some accompanying ground-state control. We have observed that p-CF_3 groups on the amino ketones significantly enhance internal quenching rate constants,[43] so we can conclude that the kinetics for the phenyl aminoalkyl ketones are dominated by conformational equilibria.

The fact that the kinetics so accurately parallel known ground-state conformational preferences says two important things about these CT interactions. The simple model of HOMO and LUMO overlap must be

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substantially correct; and the two n orbitals must overlap enough that the system actually feels some of the strain of the corresponding cycloalkane. The latter conclusion can be deduced independently from the steric effects observed in CT quenching.[27,40,41] Of course, orbital size dictates the distance required for effective overlap. In this regard, the differences between RS and R_2N are quite significant.

The thiyl group is actually a more effective quencher than the amino group, especially when attached α to the carbonyl, where RS is a rapid quencher despite the four-atom ring involved. This difference is probably due to the longer "reach" of the sulfur's 3p lone pair compared to the nitrogen's sp^3 lone-pair orbital. In fact, k_{intra}/k_{inter} for SR remains larger than that for NMe_2 for $n = 2$–4. This ratio represents the "effective molarity"[44] of a quencher and is known to vary with the geometry of the interaction,[45] in this case increasing with the spatial reach of the donor orbital. The enhanced internal reactivity of RS seems to fall off with increasing n, suggesting ever increasing importance of entropic effects. Unfortunately, we could not measure k values for SR when $n > 5$ because the competing Norrish type II reaction used to monitor triplet decay is too efficient.
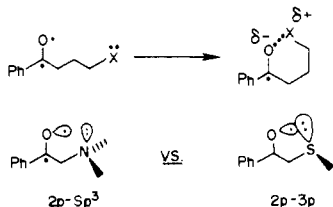
When X is vinyl, overlap with π orbitals becomes important in quenching. The interaction again is CT in nature and bimolecular quenching is not intrinsically rapid for 1-alkenes.[40] The only case where intramolecular quenching is rapid is for β-vinyl ketones. γ-Vinyl ketones undergo type II reaction in high efficiency;[46] their triplet lifetimes indicate that charge-transfer rate constants can be at most 10% as large as for the β-vinyl ketones. Thus there is a sharp contrast between the behavior of the n donors and of vinyl when n changes from 2 to 3.

The unique internal quenching ability of vinyl groups when attached β is strikingly similar to the relative efficiencies of remote double-bond participation in ester solvolyses, where the 5-hexenyl system shows much greater participation than either the 4-pentenyl[47] or the 6-heptenyl.[48] Just as for double-bond participation in solvolysis,[49] double-bond quenching of triplet ketones is accelerated multiplicatively by each additional alkyl group on the double bond.[36,40,50] Both processes involve fairly symmetric overlap of the electron-deficient reaction center with the π orbital of the double bond rather than bonding to one end. Therefore the CT

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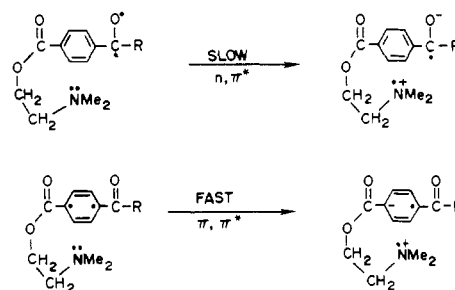(46) Wagner, P. J.; Kemppainen, A. E. *J. Am. Chem. Soc.* 1972, *94*, 7495.

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Scheme VI

complex responsible for intramolecular triplet quenching must assume a sort of bicyclic geometry. The strong parallel with known ground-state behavior again indicates the closeness required between donor and acceptor centers for effective quenching.
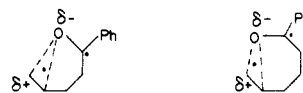
Regioelectronic Control of Charge-Transfer Quenching

If the half-empty n orbitals in n,π^* triplets are indeed as localized as the above considerations suggest, and if substantial HOMO–LUMO overlap is required for charge-transfer quenching, then internal CT quenching may not occur in molecules that cannot assume any conformation suitable for charge-transfer interaction (i.e., $\chi_F = 0$). The 4-benzoylpiperidine discussed above[27] is one of only a few such cases. Any intramolecular quenching of the triplet carbonyl by the remote amine function occurs at a rate significantly slower than 10^7 s^{-1}, less than 10^{-3} the rate observed in acyclic γ-dialkylamino ketones. Such selectivity may be called "regioelectronic" in analogy to the accepted usages of the terms "regioselective", "stereoselective", and "stereoelectronic".

We recently reported that the regioselectivity of internal charge-transfer quenching in some amino ketones depends dramatically on the electronic configuration of the lowest triplet.[51] For R = phenyl, the amino ketone in Scheme VI has an n,π^* triplet and shows long-lived phosphorescence comparable to that of the model methyl ester. However, when R = alkyl, the lowest triplet is π,π^* and internal quenching is very rapid, $k > 5 \times 10^8$ s^{-1}. Since the half-empty HOMO of the excited acceptor is a π-orbital heavily localized on the benzene ring, overlap is possible with the donor lone-pair orbital on nitrogen. In the benzophenone, $k \leq 10^5$ s^{-1}; the nitrogen lone pair cannot reach the carbonyl for any kind of effective overlap. The situation is comparable to that found by Winnik for ω-unsaturated esters of p-benzoylbenzoic acid.[52]
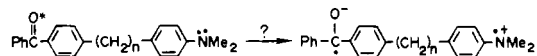
Mataga and co-workers have studied the flash kinetics of several anilinobenzophenone derivatives.[53] For three compounds ($n = 1$–3) they report appearance either of hydroxy radicals (in benzene) or of ketyl radical anions (in acetonitrile) less than 1 ns after excitation. In contrast to our suggestion of strong regioselective requirements, they conclude that both electron

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transfer and hydrogen transfer proceed *intramolecularly*, even though no contact is possible between N and C=O!

$$Ph\overset{O^*}{\overset{\|}{C}}-\langle\text{ }\rangle-(CH_2)_n-\langle\text{ }\rangle-\ddot{N}Me_2 \xrightarrow{\text{ ? }} Ph-\overset{O^-}{\underset{:}{\overset{\|}{C}}}-\langle\text{ }\rangle-(CH_2)_n-\langle\text{ }\rangle-\overset{\cdot+}{N}Me_2$$

These results probably do not invalidate our simple picture of regioelectronic selectivity, since the anilino ketone system is far more complicated than ours. Uncatalyzed hydrogen transfer requires much closer approach of O and C–H bonds than these anilinobenzophenones can possibly allow. Some form of bimolecular interaction appears to be required for hydroxy radical formation and might also allow some or all of the electron transfer. Some ground-state complexation is evident in the UV absorption of all the anilino ketones.[54] It is very possible that the majority of these bifunctional molecules are isolated and give no transients, while the minority that exist as dimeric complexes are responsible for the transients observed. To further complicate interpretation, the aniline system is the stronger UV chromophore in the anilino ketones. Since the nitrogen lone pair in aniline is strongly delocalized over the benzene ring, electron transfer from excited aniline to the ketone involves conformationally accessible overlap of both benzene rings' π systems.

Concluding Remarks

Intramolecular hydrogen abstraction by ketones has provided examples of all the limiting conditions involving competitive excited-state reaction and bond rotation. Many research groups have been studying such competitions in order to obtain otherwise inaccessible conformational information. As the last section indicates, there remains much to be understood about intramolecular bifunctional interactions of excited states, especially when extensive π systems are involved. I hope that the simple picture that has emerged from study of n–n and n–π CT interactions will provide a framework for better interpreting the complexities of larger donor and acceptor systems.

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