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Regiospecific Intramolecular Reaction of an Alkene Group with the Benzene Ring of a Triplet Ketone

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It is well-known that benzene rings undergo efficient intramolecular photocycloaddition to double bonds only when the two unsaturated groups are separated by three connecting atoms.[1-3] We have now measured the kinetic differentials responsible for such selectivity in the intramolecular quenching that occurs in triplet ketones substituted para with unsaturated hydrocarbon chains. In so doing, we have discovered a previously unrecognized intramolecular reaction between the benzene ring of a triplet phenyl ketone and a double bond, which reaction causes both cis–trans isomerization of the double bond and cycloaddition to the benzene ring. Scheme I summarizes the structures studied.

The various unsaturated ketones were all prepared by S_N2 displacements on haloalkenes with *p*-acylphenolate anion. Our initial motive was to determine whether intramolecular quenching of π,π^* triplets might occur, analogous to that observed with aminoketones.[4] Degassed acetonitrile solutions of the valerophenones were irradiated at 313 nm, and the quantum yields of corresponding acetophenone were measured. These experiments were performed at various ketone concentrations (quantum yields decrease with increasing concentration) and in the presence of varying concentrations of the triplet quencher 2,5-dimethyl-2,4-hexadiene. The latter data provided linear Stern–Volmer plots. Table I lists all the results obtained at 0.01 M ketone concentration.

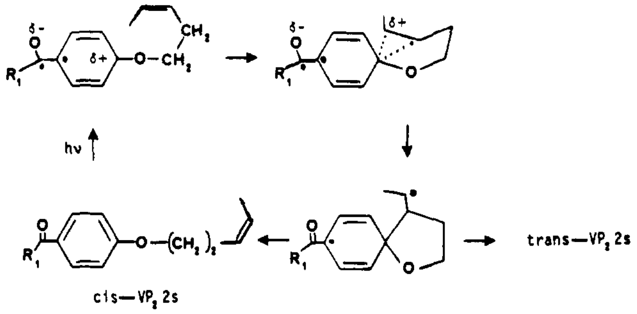
The rate constants in the table were calculated from the usual expression $k_H = \phi/\tau$ under conditions where none of the type II biradical reverts to ground-state ketone.[5] The uniformity of the value for k_H, the rate constant for γ-hydrogen abstraction, for all the ketones studied attests to the internal consistency of these data. The exact process that determines the value of k_d for *p*-alkoxy ketones is not known,[6] but it appears to be characteristic of the chromophore such that we can assume a constant value for k_d. Since alkenes are known to quench triplet ketones by a charge-transfer process,[7,8] we conclude that any decrease in quantum yield below 0.17 and any $1/\tau$ value greater than 2.4×10^6 represents CT quenching by a double bond, with rate constant k_{CT}.

The concentration dependence of quantum yields indicates that some bimolecular quenching takes place. Plots of quantum yields as a function of ketone concentration[5] provide the following values for k_q: 2, 6.5, and 30 ($\times 10^7$) $M^{-1}\ s^{-1}$ for VP_11, VP_12, and VP_13, respectively. Since these rate constants increase with increasing substitution on the double bond as reported for quenching by alkenes,[7b,8] we conclude that this bimolecular quenching represents the expected quenching of one triplet ketone molecule by the double bond on another ketone molecule and contributes increments of 0.2, 0.65, and 3.0 ($\times 10^6$) s^{-1} to the $1/\tau$ values measured at 0.01 M ketone for mono-, di-, and trisubstituted alkenes, respectively.

The total k_{CT} values in the table equal $1/\tau - k_H - k_d$. For the ketones with $n = 1$, the measured values are within experimental error of the measured bimolecular quenching rates. For the ketones with $n = 4$ and 9, there also is no evidence for any measurable *intramolecular* quenching. However, for $n = 2$ and 3, the k_{CT} exceed those expected for only bimolecular quenching. The intramolecular k_{CT} values for VP_31 and VP_33 are 2.4 and 3.5 ($\times 10^6$) s^{-1}, respectively, whereas the values for all four VP_2x compounds equal or exceed $10^8\ s^{-1}$.

It is clear that there is a tremendous regioselectivity favoring $n = 2$ in the intramolecular quenching process, the quantitative extent of which has not been measured before. Winnik has shown that the n,π^* triplets of benzophenones substituted para with unsaturated hydrocarbon tails do not undergo any intramolecular quenching until the tail is long enough (greater than or equal to nine carbons) to reach around the benzene ring to the carbonyl oxygen.[9] However, *p*-alkoxyphenyl alkyl ketones are known to have π,π^* lowest triplets.[6a,10] Therefore, the double bond can act as an electron donor to the excited benzene ring itself (as already noted for similar aminoketones[4]). The behavior of these valerophenone derivatives might thus seem to fit best with the $n = 3$ rule for π-overlap shown by diarylalkanes,[11] except for the paucity of previous examples for reaction of *triplet* benzenes with alkenes. However, it turns out that the ketones that show internal quenching also produce intramolecular chemistry.

Irradiation of the *cis*-VP_22s compound results in efficient isomerization of the double bond, $\Phi_{cis-trans} = 0.27$. Since the kinetics demand that the triplet carbonyl undergoes >99% internal quenching by the double bond, the presumed CT interaction must lead to breaking of the double bond. Earlier studies[12,13] established that ketone-sensitized isomerization of alkenes involves primarily revertible chemical addition to the double bond. Since both electron transfer and triplet energy transfer are far too endothermic to occur in this system with such large rate constants, we must conclude that the benzene ring bonds to the alkenes. The dual 1,4-biradical[14] and charge-transfer[15] nature of phenyl ketone π,π^* triplets plus the preference for five-member rings in olefin CT interactions[16,17] and in radical cyclization[18] together suggest addition specifically by the para carbon.



All of the ketones with $n = 2$, their ortho isomers, the corresponding acetophenones, and VP_31 undergo photocycloaddition

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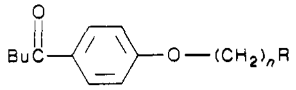
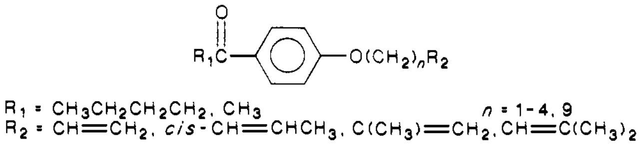
Table I. Photokinetic Data for *p*-Alkenoxyvalerophenones[a]



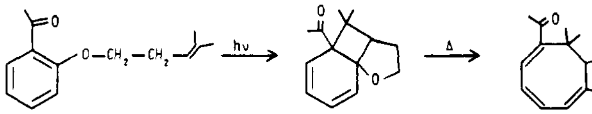
ketone[b]	n	R	Φ[c]	$k_q\tau$, M	$1/\tau$[d,e]	k_H[e]	k_d[e]	k_{CT}[e,f]
VP	0	CH_3[g]	0.17	4100	2.4	0.4	2.0	
VP_11	1	$CH{=}CH_2$	0.15	3700	2.7	0.4	2.0	0.3
VP_12	2	$CH{=}CHMe$	0.14	3300	3.1	0.4	2.0	0.7
VP_13	3	$CH{=}CMe_2$	0.045	1600	6.2	0.3	2.0	4.0
VP_21	2	$CH{=}CH_2$	0.003	110	91	0.3	2.0	89
VP_22u	2	$C(Me){=}CH_2$	0.0037	82	122	0.4	2.0	120
VP_22s	2	*cis*-$CH{=}CHCH_3$	0.0016					240[h]
VP_23	2	$CH{=}CMe_2$	0.0002					1800[h]
VP_31	3	$CH{=}CH_2$	0.06	2050	4.9	0.3	2.0	2.6
VP_33	3	$CH{=}CMe_2$	0.04	1110	9.0	0.4	2.0	6.5
VP_41	4	$CH{=}CH_2$	0.16	4350	2.3	0.4	1.9	0.1
VP_91	9	$CH{=}CH_2$	0.17	4400	2.3	0.4	1.9	0.1

[a] 0.01 M in CH_3CN, 313-nm excitation. [b] In VP_ny, y = number of alkyl groups on double bond. [c] Formation of *p*-alkoxyacetophenone. [d] $k_q = 1 \times 10^{10}$ M^{-1} s^{-1}. [e] Units of 10^6 s^{-1}. [f] Sum of intra- and intermolecular quenching by alkenyl group. [g] *p*-Methoxyvalerophenone. [h] Calculated simply from quantum yield ratios.

Scheme I



of the double bond to the benzene ring in high chemical yield and low to moderate quantum yield. Spectroscopic inspection of samples irradiated at 313 nm to varying conversions indicates that the primary photoproducts are acylbicyclo[4.2.0]octadienes.[19] Heating or GC separation (200 °C column) of these photoproducts results in quantitative rearrangement to yellow cyclooctatrienes[20] (yield = 70%, Φ = 0.05 from *p*-VP_21; 100%, 0.3 from *o*-VP_21). The cyclooctatrienes are expected thermolysis products of the bicyclo[4.2.0]octadienes. We are actively studying the structures and chemistry of the initial photoadducts more fully and shall report thereon shortly.



ortho—AP_23

These studies demonstrate that triplet as well as singlet benzenes undergo highly regiospecific intramolecular CT interactions with nearby double bonds that lead to cycloaddition products. The observed product structures indicate that the double bond adds 1,2 to the benzene ring, as has been observed for several benzonitriles.[21,22] That a π,π^* triplet is reacting is indicated by the nonreactivity of *p*-(3–butenoxy)benzophenone. Unlike the situation with excited singlets, the major addition mode appears to be stepwise and revertible, resulting in double bond isomerization. The predominance of ortho addition agrees with the CT nature of the overall excited-state interaction as well as with its triplet character.[23] The difference in state selectivity is best emphasized by the report that neither $PhOCH_2CH_2CH{=}CH_2$ nor *p*-$CH_3COPh(CH_2)_3CH{=}CH_2$ gives significant yields of cycloadducts upon 254-nm irradiation.[2]

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(19) E.g., 1-acetyl-2,2-dimethyl-6-oxatricyclo[5.4.0^{1,7}.0^{3,7}]undeca-8,10-diene from *o*-AP_23: ^1H NMR (C_6D_6) δ 5.69 (d of d, 1 H, $J_{11,10}$ = 9.6, $J_{9,10}$ = 5.5 Hz), 5.51 (d of d, 1 H, $J_{8,9}$ = 9.6, $J_{10,9}$ = 5.5 Hz), 5.42 (d, 1 H, $J_{10,11}$ = 9.8 Hz), 5.33 (d, 1 H, $J_{9,8}$ = 9.8 Hz), 3.8–3.6 (m, 2 H, OCH_2), 2.31 (s, 3 H, CH_3CO), 2.47 (d of d, 1 H, $J_{3,4}$ = 8.2, $J_{3,4'}$ = 1.6 Hz), 1.6–1.4 (m, 2 H, OCH_2CH_2), 1.25, 1.19 (each s, 3 H, CH_3).

(20) E.g., 4-acetyl-11-oxabicyclo[6.3.0]undeca-1,3,5-triene from *p*-AP_21: ^1H NMR ($CDCl_3$) δ 4.24, 4.16 (each m, 1 H, $J_{9,10}$ = 6.8 Hz, CH_2O) 1.83, 2.13 (each m, 1 H, $J_{9,10}$ = 6.3 Hz, OCH_2CH_2), 3.06 (br m, 1 H, $J_{8,9} \sim J_{8,7} \sim$ 6.3 Hz, CH_2CHCH_2), 2.29–2.50 (m, 2 H, $J_{7,8}$ = 6.3, $J_{6,7}$ = 6.8 Hz, $CHCH_2CH{=}$), 5.92 (d of t, 1 H, $J_{6,7}$ = 6.8, $J_{5,6}$ = 12.5 Hz, $CH_2CH{=}CH$), 6.27 (d, 1 H, $J_{6,5}$ = 12.5 Hz, $CH{=}CHC(COMe){=}$), 7.00 (d, 1 H, $J_{3,2}$ = 6.8 Hz, $MeCOC{=}CHCH{=}$), 5.40 (d, 1 H, $J_{2,3}$ = 6.8 Hz, $CH{=}CO$), 2.31 (s, 3 H, CH_3CO); UV λ_{max} (hexane) 370 nm (ϵ 4000). IR, MS, and ^{13}C NMR spectra also agree with the proposed structure.

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Conformational Effects on the Regiochemical Metalation of C_5–C_{13} *N*-Benzyllactams

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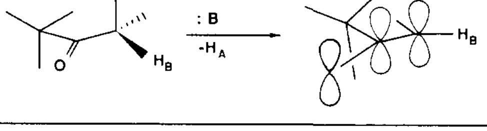
Although conformational effects have been long known to influence a variety of regiochemical and stereochemical reactions, it has not been until recently that rational approaches to controlling these important transformations have been utilized by the synthetic community. A report recently described the profound effects of conformation in medium rings on the enolization and ultimately the stereochemical outcome of alkylation.[1] An earlier report by Fraser[2] describes the stereoelectronic effect in a twistan-4-one wherein only one of the two α-protons is suitably placed for enolization[3] by base (eq 1).



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