TYPE I PHOTOREACTIONS OF •-ALKYL 8-OXOESTERS. NEIGHBORING GROUP EFFECT ON 1,4-BIRADICAL REACTIONS AND EFFECTIVE INTERNAL FILTER EFFECT BY THE TYPE I PHOTOPRODUCT

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Abstract - The a-alkyl β -oxoesters <u>1</u> undergo type II photoreactions. The process of back hydrogen transfer in the 1,4biradical intermediate to revert to the starting ester is suppressed because of the intramolecular hydrogen bonding between the hydroxyl and carboalkoxyl groups in the biradical intermediate. The hydrogen bonding determines the stereochemistry of 1,4-biradical cyclization. The cyclobutanols having the hydroxyl group *cis* to the carboalkoxyl group are formed exclusively from the a-alkyl β -oxoesters <u>1</u>. The enol form of the type II elimination product, the benzoylacetate <u>2</u>, acts as an effective internal filter for the photoreaction of the a-alkyl β -oxoester <u>1</u>.

The type II photoprocesses of phenyl ketones have been the subject of extensive investigations. The intermediacy of a 1,4-biradical is now well established. 1 The 1,4-biradical cleaves, cyclizes, or disproportionates back to the ground state ketone.² Solvation of the biradical in polar solvents enhances the type ${\rm I\!I}$ quantum vields.³ Sterically repulsive interaction between the phenyl group and the a- or Y-substituent in the transition state for 1,4-biradical cyclization enhances the formation of the trans-cyclobutanol. 3,4 We report here that the process of back hydrogen transfer in the biradical intermediate is suppressed in the type IIreaction of the a-alkyl 8-oxoester 1 because of an intramolecular hydrogen bonding between the hydroxyl and carboalkoxyl groups in the 1,4-biradical intermediate, and that the intramolecular hydrogen bonding determines the stereochemistry of 1,4biradical cyclization. The type II elimination of the a-alkyl 8-oxoester <u>1</u> gives the benzoylacetate 2 which exhibits the keto-enol tautomerism. We also report here that the enol form of the benzoylacetate $\underline{2}$ acts as an effective internal filter for the photoreaction of the a-alkyl B-oxoester 1.

Irradiation of methyl 2-benzoyl-4-methylvalerate (<u>1a</u>) in benzene under nitrogen with a 450 W high-pressure mercury lamp through a Pyrex filter gave methyl benzoylacetate (<u>2a</u>), methyl c-2-hydroxy-3,3-dimethyl-2-phenyl-r-1-cyclobutanecarboxylate (<u>3a</u>), and methyl 4-benzoyl-4-methylvalerate (<u>4a</u>) in 83, 8, and 1 % yields, respectively. The structure and the configuration of the cyclobutanol <u>3a</u> were elucidated by spectral data and elemental analysis. The ir spectrum of a dilute solution of <u>3a</u> in carbon tetrachloride showed the characteristic hydroxy and carbonyl absorptions at 3480 and 1715 cm⁻¹, respectively. Rather lower frequency at 1715 cm⁻¹ indicates that the ester carbonyl group is located so that the carbonyl oxygen forms a hydrogen bonding to the adjacent hydroxyl group. Similar irradiation of ethyl

2-benzoyl-4-methylvalerate (1b) gave ethyl benzoylacetate (2b) and ethyl σ -2hydroxy-3,3-dimethyl-2-phenyl-r-1-cyclobutanecarboxylate (3b) in 87 and 9 % yields, respectively. A trace of ethyl 4-benzoyl-4-methylvalerate (4b) could also be detected. The ir absorption of the carbonyl group in <u>3</u>b appeared at 1710 cm⁻¹, indicating that the hydroxyl group is located cis toward the carboethoxyl group. No isomeric cyclobutanols (5) which have the hydroxyl group trans to the carboalkoxyl group could be obtained in photolyses of <u>la</u> and <u>lb</u>. On the other hand, irradiation of ethyl 4-benzoyl-4-methylvalerate 4b under the same conditions gave the cyclobutanol (5b) and isobutyrophenone (6) in 26 and 35 % yields, respectively.⁵ The ir spectrum of 5b in carbon tetrachloride showed the characteristic absorptions for the free ester carbonyl group and the free hydroxyl group at 1730 and 3600 cm^{-1} . respectively. In the nmr spectrum in hexadeuteriobenzene, the hydroxylic proton of 5b appeared at \$ 2.48 in 0.090 M solution and \$ 2.30 in 0.025 or 0.012 M solution, whereas that of 3a or 3b appeared at \$ 3.08 or 3.35, respectively, regardless of concentrations. These results suggest that the hydroxylic proton of 5b forms an intermolecular hydrogen bonding at higher concentrations and that the hydroxylic proton of 3a or 3b forms an intramolecular hydrogen bonding to the carboalkoxyl group, indicating that the hydroxyl group is trans in 5b and cis in 3a or 3b with respect to the carboalkoxyl group. The nmr spectrum of <u>3b</u> showed two singlets at § 0.62 and 1.28 attributable to the C_3 -methyl groups. The C_3 -methyl groups in the cyclobutanol <u>5b</u> appeared at 5 0.55 and 1.18 as singlets. The following chemical evidence substantiates the assignment of the stereochemistry of 3b and 5b. The cyclobutanol 3b rearranged easily and quantitatively to the 3-oxoester 4b by heating in benzene. On the other hand, the cyclobutanol 5b was hardly converted to the 8-oxoester under the same conditions. The cyclobutanol 5b rearranged quantitatively to the δ -oxoester <u>4b</u> by refluxing in benzene containing acetic acid. The ease of the rearrangement of <u>3b</u> is interpreted by reference to a six-membered cyclic transition state which is achieved by the cis-relationship between the hydroxyl group and the carboethoxyl group.

Formation of the benzoylacetate 2 and the cyclobutanol 3 can be explained in terms of type II elimination and cyclization of the α -alkyl B-oxoester 1. Formation of the 8-oxoester 4 can be explained in terms of thermal rearrangement of the cyclo-



4b

butanol 3. The formation of 2, 3, and 4 from <u>la</u> and <u>lb</u> was effectively quenched by 1,3-pentadiene, suggesting that the reaction takes place from the triplet state.

Irradiation of ethyl 2-benzoylvalerate (1c) gave ethyl benzoylacetate (2b), ethyl c-2-hydroxy-3-methyl-2-phenyl-r-1-cyclobutanecarboxylate (1:1 mixture of the cis-3methyl isomer 3c and the trans-3-methyl isomer 3c with respect to the phenyl), and ethyl 4-benzoylvalerate (4c) in 82, 10, and 3 % yields, respectively. The cyclobutanol $\underline{3c}$ which has the C3-methyl group dis to the phenyl group could be separated from the mixture of $\underline{3c}$ and $\underline{3c}$ ' by repeated column chromatography. However, the cyclobutanol $\underline{3c}^{+}$ which has the C $_{3}^{-}$ methyl group trans to the phenyl group could not be isolated. The cyclobutanol $\underline{3c}^+$ is probably so unstable as to be converted to the 4oxoester 4c during the repeated chromatography. The mixture of 3c and 3c' as well as 3c was converted quantitatively to the 4-oxoester 4c by heating in benzene. Both 3cand the mixture of 3c and 3c' showed the carbonyl absorption at 1710 cm⁻¹ in their ir spectra in carbon tetrachloride. In the nmr spectrum of <u>3c</u>, the hydroxylic proton appeared at § 3.50 regardless of concentration. Substraction of the nmr spectrum of 3c from that of the mixture of 3c and 3c' gives the spectrum of 3c' which is consistent with the proposed structure and geometry. The nmr spectrum of $\underline{3c}$ showed a doublet at 4-0.55 attributable to the C₃-methyl group. The C₃-methyl group in <u>3c</u>' in the nmr spectrum obtained by the operation as described above appeared at 6 1.11. In the cyclobutanois, the methyl group cis to the phenyl group appears at higher field than the trans methyl group.⁴ Irradiation of ethyl 2-benzoylbutyrate (<u>1d</u>) gave ethyl benzoylacetate (2b) and ethyl 4-benzoylbutyrate (4d) in 87 and 10 % yields, respectively. In this case, the cyclobutanol <u>3d</u> could not be obtained. The cyclobutanol <u>3d</u> is probably so unstable under experimental conditions as to be converted to the 3-oxoester 4d.

The rate of rearrangement of the cyclobutanol $\underline{3}$ to the 4-oxoester $\underline{4}$ is affected by the C_3 -methyl group. The cyclobutanol $\underline{3b}$ was converted quantitatively to the 3-oxoester $\underline{4b}$ by heating in benzene with the rate constant of $6.8 \times 10^{-6} \text{ sec}^{-1}$ (at $60\ ^\circ$ C). The cyclobutanols $\underline{3c}$ and $\underline{3c'}$ were converted to the 4-oxoester $\underline{4c}$ with the rate constants of $8.8 \times 10^{-6} \text{ sec}^{-1}$ and $5.7 \times 10^{-4} \text{ sec}^{-1}$, respectively. The C_3 methyl group cia to the phenyl group obviously prevents the opening of the cyclobutane ring. The C_3 -methyl effect can be explained in terms of the electronic stabilization of the transition state for ring opening of the cyclobutanol $\underline{3}$ by the conjugation of the C_1 - $C_2 \circ$ bond with the phenyl group.⁶ The σ -p overlapping is maximum when p-orbitals in the phenyl group are parallel to the C_1 - $C_2 \circ$ bond as shown in A, and minimum when the p-orbitals are orthogonal to the C_1 - $C_2 \circ$ bond as shown in B (Figure 1). The conformation A is not favored in the cyclobutanol having the C_3 -methyl group cia to the phenyl group because of the sterically repulsive interaction.



(A)

(B)

Figure 1. Effect of phenyl *-orbitals on cyclobutane ring opening.

The stereospecific formation of cyclobutanols having the hydroxyl group *cis* to the carboalkoxyl group can be explained in terms of the neighboring group effect on 1,4-biradical cyclization. The hydroxyl group in the 1,4-biradical intermediate is expected to be located so that the proton forms an intramolecular hydrogen bonding to the carbonyl oxygen of the carboalkoxyl group. The hydrogen bonding is expected to affect the stereochemistry of 1,4-biradical cyclization.² Evidence for the formation of the intramolecular hydrogen bonding could be obtained by the following

experiment. Reverse transfer of the hydroxylic hydrogen to the v-radical site to give the ground state ketone is one of the possible processes of the 1,4-biradical intermediate.² An added alcohol such as *tert*-butyl alcohol solvates the biradical so as to suppress reverse hydrogen transfer, and enhances the quantum yields for type II reactions.^{2,3,7} The quantum yield for disappearance of the starting ester was measured. Degassed benzene solutions of <u>1b</u> were irradiated with 313 nm light for various periods. The quantum yield decreased with



increasing conversion (Figure 2). The decrease of the quantum yield with increasing conversion can be attributed to the internal filter effect of the enol form of the product benzoylacetate. In the photoreaction of the 4-oxoamide, its enol form acts as an internal filter.⁸ The

intercept in Figure 2 yields the true quantum yield for disappearance of <u>1b</u>, the value of which is unity indicating the complete absence of revere hydrogen transfer and hence the presence of the intramolecular hydrogen bonding in the 1,4-biradical.

Examination of the dependence of the rate of disappearance of $\underline{1}$ on irradiation time provides evidence for 100 % effective internal filtering by the enol form of the product benzoylacetate $\underline{2}$. Equation 1 describes the dependence of the amount of disappeared ester x on time t, where [K] is the initial concentration of the starting ester, y is the chemical yield of the



Figure 2. Dependence of quantum yield for disappearance of 1b in benzene on conversion.

product benzoylacetate, ϵ , ϵ' , and ϵ'' are absorption coefficients for the starting ester, the keto and enol forms of the benzoylacetate in benzene at 313 nm, respectively, ϵ is the enol content of the benzoylacetate in benzene, \bullet is the true quantum yield for disappearance of the starting ester, and I is the absorbed light intensity. The enol content ϵ could be determined to be 0.37 by nmr analysis of ethyl benzoylacetate in benzene- d_6 . The UV absorption coefficients of the α -alkyl β oxoester 1b and ethyl benzoylacetate in benzene at 313 nm are 230 and 1920, respec-

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$$\frac{d[K-x]}{dt} = \frac{c[K-x] + c'[x]y(1-e)}{c[K-x] + c'[x]y(1-e) + c''[x]ye} \bullet I$$

$$\bullet It = \{1 - \frac{c"ye}{c - c'y(1-e)}\} [x] - \frac{cc"ye[K]}{(c - c'y(1-e))^2} In\{1 - \frac{c - c'y(1-e)}{c[K]}\} \dots (1)$$

tively. The absorption coefficient of non-enolizable ethyl 2,2-dimethylbenzoylacetate in benzene at 313 nm is 80. The absorption coefficient of the keto form of benzoylacetone is reported to be ca. 50 at 310 nm.⁹ Therefore, we can estimate the absorption coefficient of the keto form of ethyl benzoylacetate in benzene at 313 nm as maximum 80. Using this value, the coefficient of the enol form of ethyl benzoylacetate can be calculated to be 5050. The irradiation times were corrected for varying intensities by using the valerophenone actinometer. The solid line in Figure 3 obtained from the Equation 1 indicates the expected disappearance on conversion



Figure 3. Rate of disappearance of 0.05 M ethyl 2-benzoyl-4-methylvalerate 1b as a function of time. Solid line is the rate predicted by equation 1 for complete internal filtering by the enol form of ethyl benzoylacetate product; dashed line indicates the expected rate without internal filtering; **0**, observed values.

when the enol form of ethyl benzoylacetate is a 100 % effective internal filter. The dashed line in Figure 3 indicates the expected rate for starting ester disappearance without internal filter. The fair agreement of the experimental data with the solid line in Figure 3 indicates that the enol form of the benzoylacetate acts as a 100 % effective internal filter in the photoreaction of the α -alkyl B-oxoester <u>1</u>. In the type II reaction of valerophenone, product acetophenone does not act as an effective internal filter and the type II quantum yield in benzene is constant.⁷ This suggests that the keto form of the product benzoylacetate does not act effectively as an internal filter.

In conclusion, the a-alkyl β -oxoesters <u>1</u> undergo type II photoreactions from the triplet state. The reverse hydrogen transfer process in the 1,4-biradical inter-

mediate is suppressed because of the intramolecular hydrogen bonding between the hydroxyl and carboalkoxyl groups in the biradical intermediate. The intramolecular hydrogen bonding determines the stereochemistry of 1,4-biradical cyclization. The enol form of the type I photoelimination product, the benzeylacetate, acts as an effective internal filter. The real quantum yield for disappearance of the starting ester is unity. The observed quantum yield decreases from unity with increasing conversion because of internal filtering by the product.

EXPERIMENTAL

Melting points were uncorrected. IR spectra were recorded on a JASCO A-3 spectrometer in carbon tetrachloride dilute solution. UV spectra were recorded on a JASCO HUM-790 spectrometer. 'H NMR spectra were recorded on a JEOL FX-900 spectrometer in hexadeuteriobenzene using tetramethylsilane as an internal standard. 'C NMR spectra were recorded out a USACO Spectrometer in deuterochloroform. Irradiations were carried out with an Ushio 450 W high-pressure mercury lamp.

Chemicals. The α -alkyl β -oxoesters <u>la-d</u> were prepared according to the reported methods."

Photolysis of 1. A typical procedure is described. A solution of ca. 2 mmol of 1 in 50 cm² of benzene was irradiated for ca. 3 hr under nitrogen using a Pyrex filter. After removal of the solvent in parks at below 20°C, the residue was flash-chromatographed" on silica gel. Elution with a mixture of benzene and ethyl acetate gave benzoylacetate 2, cyclobutanol 3, and 6-oxoester 4. The benzoylacetate 2 and the 6-oxoester 4 were identified by direct comparison with the authentic samples." Physical properties of all new products are shown below.

Methyl c-2-hydroxy-3.3-dimethyl-2-phenyl-r-1-cyclobutanecarboxylate (3a): mp 85-86 °C; IR 3480 and 1715 cm⁻¹; ¹H NMR ϵ 0.61 (3H, s, CH,), 1.27 (3H, s, CH,), 1.66 (1H, d of d, J-8.8 and 10.8 Hz, 4-H), 2.42 (1H, d of d, J=9.5 and 10.8 Hz, 4-H), 3.08 (1H, bs, OH), 3.30 (3H, s, COOCH,), 3.60 (1H, d of d, J=8.8 and 9.5 Hz, 1-H¹, and 7.1-7.5 (5H, m, aromatic). Found: C, 71.78; H, 7.77 %. Calcd for C₁, H₁₀0,: C, 71.77; H, 7.74 %.

Ethyl c-2-hydroxy-3, 3-dimethyl-2-phenyl-<math>n-1-cyclobutanccarboxylate (3b): mp 42-43 C; IR 3480 and 1710 cm⁻¹; 'H NMR 5 0.62 (3H, s, CH,), 0.91 (3H, t, J=7.1 Hz, CH,CH,), 1.28 (3H, s, CH,), 1.72 (1H, d of d, J=8.8 and 10.6 Hz, 4-H), 2.45 (1H, d of d, J=9.5 and 10.6 Hz, 4-H), 3.35 (1H, bs, OH), 3.61 (1H, d of d, J=8.8 and 9.5 Hz, 1-H), 3.91 (2H, q, J=7.1 Hz, CH,CH,), and 7.1-7.4 (5H, m, aromatic); "C NMR 6 14.18 (q), 21.92 (q), 26.08 (q), 34.15 (t), 40.71 (d), 41.75 (s), 60.48 (t), 82.07 (s), 125.97 (2d), 127.33 (d), 128.05 (2d), 142.88 (s), and 173.18 (s). Found: C, 72.51; H, 8.15 %. Calcd for C_{14}H_{4}O; C, 72.55; H, 8.12 %.

Ethyl c-2-hydroxy-t-3-methyl-2-phenyl-r-1-cyclobutanecarboxylate (3c)t: IR 3480 and 1710 cm⁻¹; ¹H NMR & 0.55 (3H, d, J=6.8 Hz, CH,), 0.94 (3H, t, J=7.0 Hz, CH,CH,), 1.2-1.6 (1H, m, 4-H), 2.4-2.9 (2H, m, 3-H and 4-H), 3.50 (1H, bs, OH), 3.57 (1H, d of d, J=5.4 and 9.0 Hz, 1-H), 3.93 (2H, q, J=7.0 Hz, CH,CH,), and 7.0-7.5 (5H, m, aromatic).

Ethyl a-2-hydroxy-a-3-methyl-2-phenyl-r-1-cyclobutanecarboxylate (3c')#: IR^{##} $3480 and 1710 cm⁻⁺; 'H NMR^{###} <math>\in$ 0.90 (3H, t, J=7.0 Hz, CH,CH,), 1.11 (3H, d, J=6.8 Hz, CH,), 2.0-2.3 (1H, m, 4-H), 2.4-2.9 (2H, m, 3-H and 4-H), 3.4-3.6 (1H, m, 1-H), 3.50 (1H, CH), 3.88 (2H, q, J=7.C Hz, CH,CH,), and 6.9-7.2 (5H, m, aromatic).

Photolysis of <u>4b</u>. A solution of 2 mmol of <u>4b</u> in 50 cm' of benzene was irradiated under nitrogen using a Pyrex filter. Treatment of the irradiation mixture by the similar manner to the case of <u>1</u> gave the cyclobutanol <u>5b</u> and isobutyrophenone 6.

Ethyl t-2-hydroxy-3,3-dimethyl-2-phenyl-r-1-cyclobutanecarboxylate (5b)t: IR 3600 and 1730 cm⁻¹; 'H NMR & 0.55 (3H, s, CH,), 0.72 (3H, t, J=7.2 Hz, CH,CH,), 1.18 (3H, s, CH,), 1.74 (1H, d of d, J=9.7 and i1.2 Hz, 4-H), 2.16 (1H, d of d, J-9.7 and 11.2 Hz, 4-H), 2.30 (1H, bs, OH in dilute solution), 3.34 (1H, t, J=9.7 Hz, 1-H), 3.82 (2H, q, J=7.2 Hz, CH,CH,), and 7.0-7.6 (5H, m, aromatic); ''C NMR & 13.86 (q), 24.39 (q), 24.85 (q), 31.61 (t), 42.14 (s), 50.40 (d), 60.10 (t), 82.27 (s), 125.38 (2H), 126.88 (d), 127.72 (2d), 142.10 (s), and 172.90 (s).

Determination of Quantum Yield for Disappearance of <u>1b</u>. The degassed 0.05 M solution of <u>1b</u> was irradiated on a merry-go-round apparatus using a potassium chromate filter solution to isolate 313 nm light. Reactant concentration was measured at regular time intervals on a Shimazu GC-4B gas chromatograph.

*The cyclobutanol <u>3c</u> and <u>5b</u> are liquid. Complete purification of them could not be achieved because these cyclobutanols changed quantitatively to δ -oxoesters during vacuum distilation. #The cyclobutanol <u>3c</u>' was obtained as a mixture with <u>3c</u>. #These spectra are derived by substracting the spectra of <u>3c</u> from those of the mixture of <u>3c</u> and <u>3c</u>'.

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Determination of Rate Constant for Thermal Rearrangement of 3 to 4. cyclobutanol 3 in benzene-d, was sealed in an NMR tube and was heated at 60 $^{\circ}$ C. Concentrations of 3 and the product 6-oxoester 4 were measured at regular time intervals on a 'H NMR spectrometer. Prolonged heating resulted in the quantitative formation of the 4-oxoester. The rate constant for the thermal rearrangement of 3c'to 4c can be determined by using the mixture of 3c and 3c' since the nmr peaks of 3c'are characterized by substracting the nmr peaks of 3c from those of the mixture of 3cand <u>3c</u>'.

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