Photochemistry of Methyl-Substituted Butyrophenones[1]

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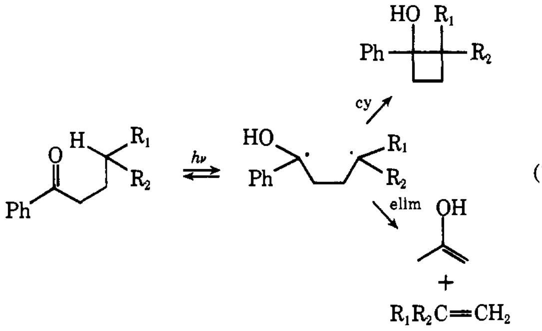
Abstract: The effects of methyl substituents upon the photochemical behavior of butyrophenone have been investigated. *tert*-Alkyl phenyl ketones undergo competitive α- (type I) cleavage and type II photoelimination and cyclization. The rate constant for α-cleavage ($\sim 1 \times 10^7$ sec^{-1}) is considerably slower than for α-cleavage of triplet *tert*-butyl alkyl ketones owing to a difference in the energetics of the reactions. The reactivity of the aromatic carbonyl triplet state toward γ-hydrogen abstraction is determined primarily by γ-substitution and is less affected by α and β substituents. α substituents increase the percentage of cyclization products whereas β substituents have the opposite effect. The effects of substituents on the behavior of the 1,4-biradical intermediates are explained in terms of the transition states for biradical cyclization and elimination.

The type II photoelimination and cyclization reactions of aryl alkyl ketones having a γ hydrogen have been the subject of extensive mechanistic investigation.[2–7] The intermediacy of a 1,4-biradical which can give rise to elimination and cyclization products as well as ground state ketone (eq 1) is now well established.[2] Whereas the effects of structure and solvent on the rate constant for γ-hydrogen abstraction and quantum yield for photoelimination have been extensively studied, much less is known about the nature of the 1,4-biradical intermediate and the factors which govern the relative rate constants for cyclization and elimination as well as the stereochemistry of cyclization.



(1)

As part of a study designed to provide information about the nature of 1,4-biradical intermediates,[8] the photochemistry of the methyl-substituted butyrophenones **1–10** has been investigated. Our results show pronounced substituent effects on biradical elimination and cyclization reactions. The *tert*-alkyl phenyl ketones **3** and **6** were observed to undergo α- (type I) cleavage as well as type II photoelimination and cyclization, thus providing the first example of competitive α-cleavage and γ-hydrogen abstraction for an aryl ketone.

Results

Product Studies. The methyl-substituted butyrophenones **1–10** were synthesized by standard procedures (see Experimental Section). Photolysis in dilute benzene solution followed by preparative vpc or silica gel chromatography yielded acetophenone (**1**, **4**, **7–10**), propiophenone (**2**, **5**), or isobutyrophenone (**3**, **6**), and the corresponding cyclobutanols as the major isolated products. The cyclobutanols all had ir spectra with OH stretching but without carbonyl absorption. Two isomeric cyclobutanols were isolated from ketones **4**, **5**, and **6** with the major product in each case having the shorter vpc retention time. The assignment of cyclobutanol stereochemistry rests primarily on the 60-MHz nmr spectra (Table I). Only the methyl proton nmr data for ketones **2–5** and **9** are included in Table I since the rest of the spectrum did not aid the stereochemical assignments. The only cyclobutanol from **2** had a vpc retention time and nmr spectrum identical with those of the major cyclobutanol from **4**, which has previously been assigned trans stereochemistry.[3,5] The cis methyl in the minor cyclobutanol from **4** is at higher field than the trans methyl. This observation provides the basis for the assignments of the cis and trans methyl groups for **3**, **5**, and **6**. The assignment of the stereochemistry of the two cyclobutanols from **6** is corroborated by the effect of the shift reagent Eu(DPM)$_3$[9] upon the nmr spectra (Table I). The minor (cis) isomer paramagnetic shifts were greatest for the low-field (trans) methyl singlet and the methine multiplet. The methine multiplet paramagnetic shift for the major (trans) isomer is much smaller than that observed for the minor (cis) isomer. Curiously, the paramagnetic shift of the methyl doublet is about the same for both isomers. The assignment of the methylene protons is based upon the larger vicinal coupling constant for the proton trans to methine[10] and the slightly larger paramagnetic shifts for the proton cis to the hydroxyl group. No diamagnetic shifts were observed for either cyclobutanol.

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(1) (a) The authors thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, The Research Corporation, and the Merck Foundation for support of this research. (b) For a preliminary account of a portion of this work, see F. D. Lewis and T. A. Hillard, *J. Amer. Chem. Soc.*, **92**, 6672 (1970).

(2) For a recent review, see P. J. Wagner, *Accounts Chem. Res.*, **4**, 168 (1971).

(3) P. J. Wagner, *J. Amer. Chem. Soc.*, **89**, 5898 (1967).

(4) (a) P. J. Wagner and A. E. Kemppainen, *ibid.*, **90**, 5896 (1968); (b) P. J. Wagner and H. N. Schott, *ibid.*, **91**, 5383 (1969); (c) J. N. Pitts, D. R. Burley, J. C. Mani, and A. D. Broadbent, *ibid.*, **90**, 5900 (1968).

(5) J. N. Barltrop and J. D. Coyle, *ibid.*, **90**, 6584 (1968).

(6) F. D. Lewis and N. J. Turro, *ibid.*, **92**, 311 (1970).

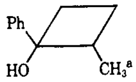
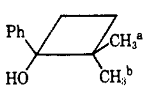
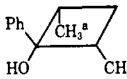
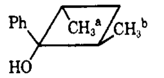
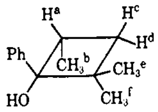
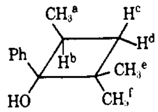
(7) F. D. Lewis, *ibid.*, **92**, 5602 (1970).

(8) For the preceding paper in this series, see F. D. Lewis and R. A. Ruden, *Tetrahedron Lett.*, 715 (1971).

(9) (a) C. C. Hinkley, *J. Amer. Chem. Soc.*, **91**, 5160 (1969); (b) P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert, *ibid.*, **92**, 5734 (1970); (c) J. K. M. Sanders and D. H. Williams, *ibid.*, **93**, 641 (1971); (d) B. L. Shapiro, J. R. Hlubucek, G. R. Sullivan, and L. F. Johnson, *ibid.*, **93**, 3281 (1971).

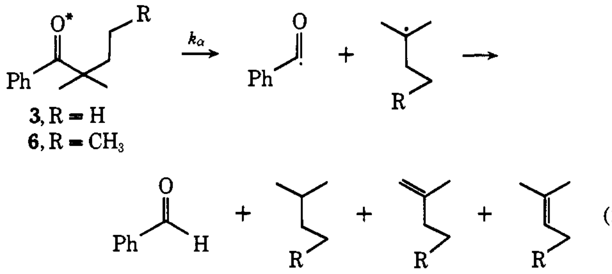
(10) J. E. Baldwin and J. A. Kapecki, *ibid.*, **92**, 4874 (1970).

Table I. Nmr Data for Cyclobutanols

Ketone	Cyclobutanol	δ, ppm[a]	Δ(Eu), cps[b]
2, **4**[c]		a 1.10 (d, J = 6.5)	
4[d]		a 0.60 (d, J = 6.5)	
3, **9**		a 0.65 (s) b 1.28 (s)	
5[c]		a 1.03 (d, J = 7.5)	
5[d]		a 1.13 (d, J = 6.8) b 0.65 (d, J = 7.0)	
6[c]		a 2.9 (m) b 1.05 (d, J = 6.8) c 1.67 (d, J = 8) d 1.65 (d, J = 10) e 0.72 (s) f 1.16 (s)	18 14 20 23 17 31
6[d]		a 0.92 (d, J = 6.8) b 2.6 (m) c 1.53 (d, J = 11) d 1.75 (d, J = 9) e 0.70 (s) f 1.22 (s)	20 66 23 26 24 43

[a] Proton chemical shifts in CCl_4 except for **6**[c] and **6**[d] in $CDCl_3$. [b] Paramagnetic shift with $Eu(DPM)_3$, 7.2% for **6**[c] and 5.8% for **6**.[d] [c] Major photocyclization product. [d] Minor photocyclization product.

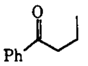
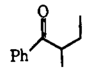
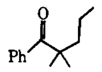
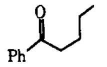
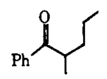
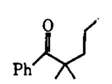
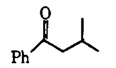
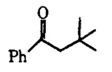
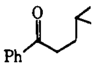
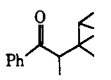
Products arising from α-cleavage (eq 2) as well as γ-hydrogen abstraction were obtained upon photolysis of the *tert*-alkyl phenyl ketones **3** and **6**. Alkane and alkene products were identified by vpc coinjection with authentic samples. Several unidentified minor products were also detected from **3** and **6**.



(2)

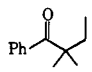
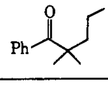
Quantum Yields. Degassed 0.05 M benzene solutions of ketones **1–10** contained in sealed Pyrex tubes were irradiated using a 450-W medium-pressure mercury lamp and a filter solution of potassium chromate to isolate the 313-nm line. Light intensities were measured by simultaneous irradiation of the ketones and benzophenone–benzhydrol actinometer solutions[11] at 25°. Product yields were determined by analytical vpc for conversions of <5%. The quantum yields for elimination (acetophenone, propiophenone, or isobutyrophenone) and cyclization (cyclobutanol) product formation are given in Table II. The type II elimination quantum yields for **1**, **4**, **7**, and **9** are in reasonable agreement with literature values[4] as are the percentage cyclization results for **1**, **4**, and **9**.[5] The quantum yields for benzaldehyde, alkane, and alkene formation from **3** and **6** in benzene and benzene containing 0.5 M hexyl mercaptan are given in Table III.

Table II. Quantum Yields and Kinetic Data for Photoelimination and Cyclization of Alkyl Phenyl Ketones

	Ketone	Φ_{elim}	Φ_{cy}[a]	% cy	$k_q\tau$, M^{-1}	$1/\tau \times 10^{-8}$ sec^{-1}
1		0.36	0.042	10	670[b]	0.075
2		0.28	0.116 t	29	390	0.13
3		0.004 0.007[c]	0.032 0.057[c]	89	260	0.19
4		0.33	0.069 t 0.022 c	22	36[b]	1.4
5		0.17	0.094 t, t 0.030 t, c	43	37	1.3
6		0.03 0.033[c]	0.044 t 0.031 c 0.081[c]	71	44	1.1
7		0.26	0.045	15	245[b]	0.20
8		0.17	0.005	3	93	0.54
9		0.24	0.041	15	11[b]	4.5
10		0.014	0.001	10	5.6	9.0

[a] Cyclobutanol stereochemistry is indicated where known. [b] Values from ref 4a. [c] Quantum yields for formation of product from the 1,4-biradical intermediate.

Table III. α-Cleavage Quantum Yields for *tert*-Alkyl Phenyl Ketones

	Ketone	Solvent	Φ_{PhCHO}	Φ_{alkane}	Φ_{alkene}
3		C_6H_6 C_6H_6–RSH[a]	0.12 0.31	0.071[b] 0.34[b]	0.137[c] 0.0
6		C_6H_6 C_6H_6–RSH[a]	0.031 0.055	0.019[d] 0.060[d]	0.030[e] 0.0

[a] n-Hexyl mercaptan, 0.5 M. [b] 2-Methylbutane. [c] 2:1 ratio of 2-methyl-1-butene:2-methyl-2-butene. [d] 2-Methylpentane. [e] 4:1 ratio of 2-methyl-1-pentene:2-methyl-2-pentene.

The 0.5 M mercaptan should scavenge virtually all noncage free radicals. Thus the quantum yields for α-cleavage product formation are approximately 0.34 for **3** and 0.06 for **6**. The quantum yield for cyclo-

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(11) W. M. Moore and M. Ketchum, *ibid.*, 84, 1368 (1962).

butanol formation, but not photoelimination, also increases with added mercaptan, an effect similar to that observed for **6** with added alcohols.[12] Photoreduction of the carbonyl excited state does not compete with α-cleavage or γ-hydrogen abstraction in the presence of 0.5 *M* mercaptan as is shown by the absence of *tert*-alkylphenylcarbinols.[13]

Rate Constants. Photolysis of all ketones except **3** and **6** in degassed benzene solution at 313 nm in the presence of varying amounts of *trans*-piperylene resulted in linear Stern–Volmer plots (Φ_0/Φ *vs.* [quencher]). The slopes of the Stern–Volmer plots are equal to $k_q\tau$ (Table II), where k_q is the rate constant for quenching of the ketone triplet state by piperylene and τ is the triplet lifetime. Assumption of the value 5×10^9 sec^{-1} for k_q[3] allows calculation of τ or $1/\tau$ (Table II). Quenching of **3** and **6** led to nonlinear Stern–Volmer plots with benzaldehyde formation quenched much more strongly than cyclobutanol formation. Apparently the benzoyl radicals from α cleavage are scavenged by the *trans*-piperlyene. Linear Stern–Volmer plots were obtained when naphthalene was used as the quencher (366-nm irradiation).

Absorption and Emission Spectra. Ketones **1–10** all have normal aromatic carbonyl n,π^* absorption spectra with λ_{max} 320–325 nm and ϵ_{max} 41–108. The *tert*-alkyl phenyl ketones **3** and **6** have the most intense absorption. The emission spectra of ketones **1–10** in EPA all resemble that of acetophenone with E_t = 72–74 kcal. Intersystem crossing efficiencies (Φ_{st}) of **3** and **6** were determined by the method of Lamola and Hammond.[14] The 0.73 *M* *cis*-piperylene[15] used for triplet counting is sufficient to quench 99% of the triplets of **3** and 97% of the triplets of **6**, based on the kinetic results given above. The observed extents of sensitized piperylene isomerization relative to acetophenone (Φ_{st} = 1.0[15]) for **3** = 0.99 and **6** = 0.98 correspond to intersystem crossing quantum yields of 1.0 ± 0.05 for **3** and **6**.

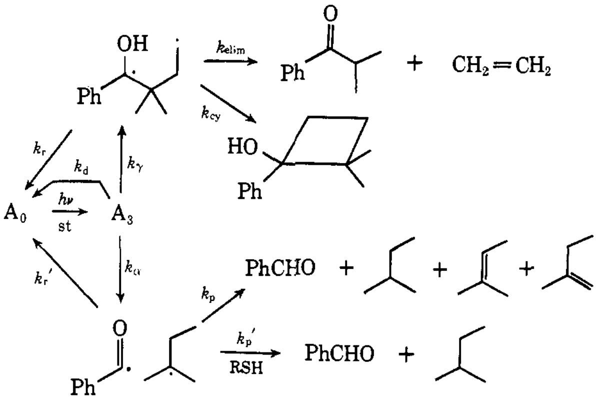
Discussion

The effects of methyl substituents upon the photochemical behavior of butyrophenone are of three important types: (a) the effect on the competition between α-cleavage and γ-hydrogen abstraction primary photoprocesses, (b) the effect on excited state reactivity, and (c) the effect on the behavior of the 1,4-biradical intermediate. The results can conveniently be discussed in terms of Scheme I, for which α,α-dimethylbutyrophenone (**3**) has been used as an example. The *tert*-alkyl phenyl ketones **3** and **6** conform to the general observation that simple alkyl phenyl ketones have high intersystem crossing quantum yields ($\Phi_{st} \sim 1.0$).[14] Phosphorescence lifetime measurements indicate that the n,π^* triplet is of lower energy than the π,π^* triplet in nonpolar media for alkyl phenyl ketones including *tert*-alkyl phenyl ketones.[16] Since ketones **1–10** all react from a lowest n,π^* triplet of approximately the same triplet energy, it seems unlikely that the observed effects of substituents are due to changes in excited state reactivity. The n,π^* triplet solution lifetime is determined by the rate constants for nonradiative decay (k_d), γ-hydrogen abstraction (k_γ), and α-cleavage (k_α, eq 3). Since k_d is $<10^6$ for aryl

$$1/\tau = k_d + k_\gamma + k_\alpha \qquad (3)$$

ketones in benzene solution,[17] $k_d \ll k_\gamma + k_\alpha$ and therefore the $1/\tau$ values in Table II equal k_γ or, for **3** and **6**, $k_\gamma + k_\alpha$.

Scheme I



Dialkyl ketones have long been known to undergo competitive type I and type II photocleavage in solution with α-cleavage sometimes predominating.[18] However, ketones **3** and **6** represent the first example of such a competition for alkyl phenyl ketones. Pivalophenone[8,19] and some benzyl phenyl ketones,[20] including α-phenylbutyrophenone, have been observed to undergo α-cleavage, indicating the necessity of forming a relatively stable alkyl free radical in order for α cleavage of alkyl phenyl ketones to occur. The sum of the quantum yields for γ-hydrogen abstraction (Table II) and α-cleavage (Table III) product formation for **3** and **6** is considerably less than unity. The observed inefficiencies are due to both cage recombination of α-cleavage radicals (k_r') and reabstraction of the 1,4-biradical to give ground state ketone (k_r). Allowing for ~30% cage recombination of benzoyl and alkyl radicals[21] the quantum yields for α-cleavage can be estimated as 0.44 for **3** and 0.08 for **6**. Since the triplet state lifetime ($1/\tau$, Table II) is determined by the rate constants for α-cleavage (k_α) and γ-hydrogen abstraction (k_γ), the rate constants for these processes can be estimated from the approximate quantum yields and are given in Table IV along with the value of k_α

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[12] P. J. Wagner, private communication.

[13] Photoreduction of *tert*-alkyl aryl ketones produces carbinols and not pinacols: F. D. Lewis and J. G. Magyar, *J. Org., Chem.*, in press.

[14] A. A. Lamola and G. S. Hammond, *J. Chem. Phys.*, 43, 2129 (1965).

[15] Use of piperylene concentrations greater than 1 *M* was purposely avoided; see R. Hurley and A. C. Testa, *J. Amer. Chem. Soc.*, **92**, 211 (1970).

[16] P. J. Wagner, M. J. May, A. Haug, and D. R. Graber, *ibid.*, **92**, 5269 (1970), and references therein.

[17] (a) F. D. Lewis, *Tetrahedron Lett.*, 1373 (1970); (b) F. D. Lewis *J. Phys. Chem.*, 74, 3332 (1970), and references therein.

[18] (a) C. H. Bamford and R. G. W. Norrish, *J. Chem. Soc.*, 1531, 1544 (1938); (b) N. C. Yang and E. D. Feit, *J. Amer. Chem. Soc.*, **90**, 504 (1968); (c) N. C. Yang, E. D. Feit, M. H. Hui, N. J. Turro, and J. C. Dalton, *ibid.*, **92**, 6974 (1970); (d) L. Lee, B. McAneney, and J. E. Guillet, *Can. J. Chem.*, **49**, 1311 (1971).

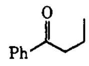
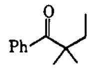
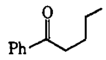
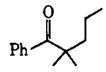
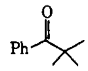
[19] H.-G. Heine, *Justus Liebigs Ann. Chem.*, **732**, 165 (1970).

[20] J. Kenyon, A. Rassoul, and G. Soliman, *J. Chem. Soc.*, 1774 (1956).

[21] A referee has suggested a maximum cage recombination efficiency of ~0.3 based on the quantum yield for decomposition of di-*tert*-butyl ketone (0.71).[18c] However, cage decarbonylation of pivaloyl radical is doubtless more efficient than that for benzoyl radical.[22a] Thus the cage recombination efficiency for benzoyl and *tert*-alkyl radicals may well be >0.3.

[22] (a) R. K. Solly and S. W. Benson, *J. Amer. Chem. Soc.*, **93**, 1592 (1971); (b) R. K. Solly and S. W. Benson, *ibid.*, **93**, 2127 (1971).

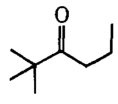
Table IV. Rate Constants for α-Cleavage and γ-Hydrogen Abstraction

	Ketone	$1/\tau \times 10^{-8}$ sec^{-1}	$k_\alpha \times 10^{-8}$ sec^{-1}	$k_\gamma \times 10^{-8}$ sec^{-1}
1		0.075[a]		0.075
3		0.19	0.084	0.10
4		1.4[a]		1.4
6		1.1	0.088	1.0
11		0.11[b]	0.11	

[a] Values from ref 4a. [b] Value from ref 13.

for pivalophenone (**11**) and the k_γ values for **1** and **4**. In view of the errors in the quantum yields, triplet lifetimes, and estimated cage recombination for **3** and **6**, the estimated rate constants k_α and k_γ for **3** and **6** are within the experimental error of the values of k_α for **11** and k_γ for **1** and **4**. Thus introduction of competition of α-cleavage with γ-hydrogen abstraction does not detectably alter the efficiency of either primary process. This should in general be the case when a competing process does not introduce a change in the reactive excited state.

Comparison of the above results with those of Yang and coworkers[18b,c] for the dialkyl ketones **12–14** reveals a significant difference between the rates of α-cleavage for dialkyl and alkyl phenyl ketones. Unlike the behavior of **3** and **6**, **12** and **13** undergo predominantely α-cleavage from their n,π* triplet states.[18b] Di-*tert*-butyl ketone (**14**) undergoes α-cleavage with a rate constant of ~8 × 10^9 sec^{-1}, over 10^2 times faster than the *tert*-alkyl phenyl ketones (Table IV). What makes this difference in rate constants most impressive is the fact that dialkyl ketones and alkyl phenyl ketones undergo γ-hydrogen abstraction from the triplet state with comparable rate constants.[2] One possible explanation of the different behavior of dialkyl and alkyl phenyl ketones follows from a consideration of the heats (standard enthalpies) of reaction for α-cleavage and 1,4-biradical formation. The $\Delta H_r°$ values in Table V were estimated using the group additivity approach of Benson.[23] Details of these calculations are given in the Appendix. The important conclusion that the phenyl group contributes to biradical stability but not to formyl radical (RCO·) stability[22,24] is not affected by the several kcal/mol error in the estimated heats of reaction. Thus, whereas α-cleavage is exothermic for dialkyl ketones (E_T ~ 78 kcal/mol), it is approximately thermoneutral for *tert*-alkyl phenyl ketones (E_T ~ 72 kcal/mol). The absence of α-cleavage from secondary alkyl phenyl ketones such as **2**, **5**, and isobutyrophenone[17a] is probably due to the fact that α-cleavage is sufficiently endothermic ($\Delta H_r°$ ~77 kcal/mol) that it cannot compete with γ-hydrogen abstraction or nonradiative decay of the triplet state in solution at room temperature. The failure of exothermic biradical formation to compete more effectively with α cleavage for both dialkyl and *tert*-alkyl phenyl ketones may indicate a sizeable entropy of activation for formation of the six-membered transition state necessary for γ-hydrogen abstraction.[25]



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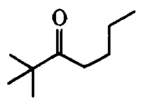

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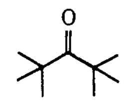

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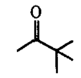
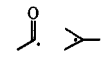
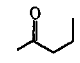
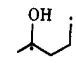
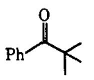
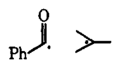
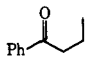
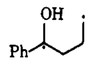
Table V. Calculated Heats of Reaction for α-Cleavage and γ-Hydrogen Abstraction

Ketone	Intermediates	$\Delta H_r°$, kcal/mol
		72
		72
		73
		66

While an explanation based on simple energetics for the large difference in dialkyl and alkyl phenyl ketone triplet n,π* reactivity toward α-cleavage is attractive by virtue of its simplicity, it may not be entirely accurate. Singlet n,π* states of dialkyl[18c] and cycloalkyl[26] ketones are at least two orders of magnitude less reactive than the triplet states, in spite of the higher excited state energies of the singlet. Other factors such as excited state electronic distribution and geometry may be important in determining excited state reactivity toward α-cleavage. Lack of knowledge about such excited state properties of large carbonyl compounds makes further speculation unwarranted.

The triplet state lifetimes (Table II) for all ketones except **3** and **6** are determined by the rate constant of γ-hydrogen abstraction ($1/\tau = k_\gamma$). Combining the values of $1/\tau$ in Table II with the estimates for k_γ in Table IV, several conclusions can be reached. First, k_γ is determined primarily by the degree of substitution at the γ carbon and reflects the strength of the γ C–H bond being broken.[2,4] β substituents do increase k_γ (compare **1**, **7**, and **8**); however, the increase is only slightly larger than the statistical correction for the number of abstractable γ hydrogens. Even without such a statistical correction, the increase in k_γ for **1** *vs.* **8** (sevenfold) is much smaller than for **1** *vs.* **9** (60-fold). The effect of α substituents on k_γ [compare **1**, **2**, **3** (Table IV) or **4**, **5**, **6** (Table IV)] is even less than that for β substituents.

The 1,4-biradical intermediates formed upon γ-hydrogen abstraction can undergo elimination, cyclization, or reversion to ground state ketone (Scheme I). Since $k_\gamma \gg k_d$, the quantum yields for product formation (eq 4, 5) are independent of the reactivity of

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(23) S. W. Benson, "Thermochemical Kinetics," Wiley, New York, N. Y., 1968.

(24) P. J. Krusic and T. A. Rettig, *J. Amer. Chem. Soc.*, **92**, 722 (1970).

(25) F. D. Lewis, R. W. Johnson, and R. A. Ruden, *ibid.*, in press.

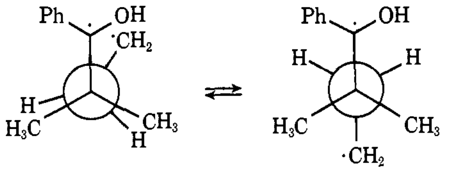
(26) J. C. Dalton, D. M. Pond, D. S. Weiss, F. D. Lewis, and N. J. Turro, *ibid.*, **92**, 2564 (1970).

$$\Phi_{\text{elim}} = k_{\text{elim}}/(k_{\text{elim}} + k_{\text{cy}} + k_{\text{r}}) \quad (4)$$

$$\Phi_{\text{cy}} = k_{\text{cy}}/(k_{\text{cy}} + k_{\text{elim}} + k_{\text{r}}) \quad (5)$$

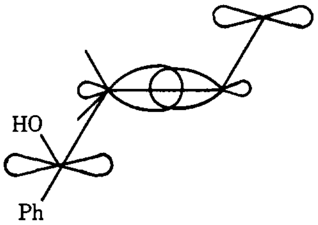
the excited state and are determined by the behavior of the biradical intermediate. The results in Table II show several notable effects of methyl substituents upon the biradical intermediates. The most dramatic of these is the increase in the percentage of cyclization upon α substitution. For example, α-methyl and α,α-dimethyl substitution of butyrophenone increases the percentage of cyclization from 10 to 29 and 89%, respectively. In contrast to the effect of α substituents, β substituents result in a small increase in the percentage of cyclization for β-methyl- and a marked decrease for β,β-dimethylbutyrophenone (compare **1**, **7**, **8**). The effect of γ substituents on the percentage of cyclization is small in comparison to α- and β-substituent effects.

The effect of α substituents is somewhat reminiscent of the increased yields and rates of cyclization observed for some ionic ring–chain equilibria when methylene hydrogens are replaced by alkyl groups.[27] The original Thorpe–Ingold explanation of such "*gem*-dialkyl" effects, based on relief of steric compression between substituents on the same carbon when a small ring is formed, is unsatisfactory in our case since α and β substituents would be expected to show the same general effect. An explanation based on more current conformational theory of the *gem*-dialkyl effect is that substituents increase the barrier to rotation about the α–β bond, thus increasing the lifetime of the originally formed cisoid biradical conformation from which cyclization and reabstraction can occur (eq 6). However, one would again expect that β substituents would show a similar effect. Furthermore, even a rigid cisoid biradical geometry does not ensure a high percentage of cyclization product.[8,25]



(6)

The observed increase in percentage cyclization with α substitution is due more to a decrease in elimination quantum yields ($\Phi_1 = 0.36$, $\Phi_2 = 0.28$, $\Phi_3 = 0.012$[28]) than to an increase in the cyclization quantum yields ($\Phi_1 = 0.042$, $\Phi_2 = 0.12$, $\Phi_3 = 0.10$[28]). Thus α substituents effectively decrease k_{elim} relative to k_{cy} and k_{r}. Similarly, the decrease in percentage cyclization is going from **7** to **8** reflects a much larger decrease in Φ_{cy} than in Φ_{elim}. These substituent effects are most readily explained in terms of the biradical conformations necessary for elimination and cyclization. Wagner[2,4a] has suggested that elimination requires continuous overlap of both radical p orbitals with the σ bond undergoing cleavage. Support for this argument has been provided by results for a number of exocyclic[29] and endocyclic[30] ketones which form a high proportion of cyclization products. In these cases the conformations of the ring systems may prevent maximum overlap of one of the radical p orbitals with the α–β bond. For acyclic biradicals such as **3** and **6** there is no geometric prevention of maximum overlap; however, 1,2-eclipsing interactions between α substituents and the hydroxyl and phenyl groups may destabilize the conformation of the biradical necessary for elimination (**15**). The magnitude of such eclipsing interactions is probably quite small and will depend upon the extent of rehybridization at the radical centers. β substituents introduce no 1,2-eclipsing interaction with phenyl and hydroxyl so elimination from **7** or **8** should not be hindered (**16**). The low quantum yield for elimination from **10** suggests that 1,2-eclipsing interactions between β and γ substituents (**17**) may also hinder elimination.



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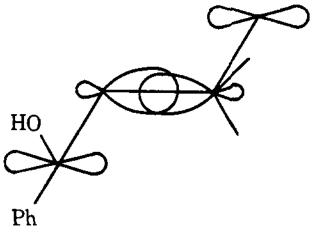

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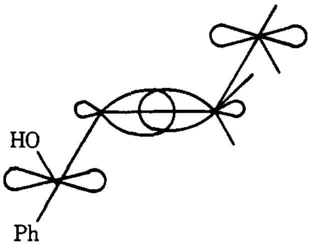

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The transition state for cyclization of a biradical intermediate requires overlap of the radical centers. Since continuous overlap of the radical orbitals with the α–β bond is not required, the carbon skeleton probably is nonplanar so as to minimize 1,2-eclipsing interactions.[31] The small variation in cyclization quantum yield (compared with that for elimination quantum yield) with α substitution suggests that eclipsing interactions destabilize the conformation for biradical cyclization (**18**) less than that for elimination (**15**). A nonplanar cyclization transition state can readily accommodate a single (equatorial) β-methyl substituent (**19**). However a second β substituent will introduce a 1,3-diaxial interaction. The importance of 1,3-diaxial interactions in cyclobutanes is shown by the fact that 1,3-cis-disubstituted cyclobutanes, in which both substituents can be equatorial, are considerably less planar than 1,3-trans-disubstituted cyclobutanes, in which one of the substituents is axial in a nonplanar conformation.[32] The low quantum yield for cyclization from ketone **10** can also be explained by the pres-

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[27] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 197.

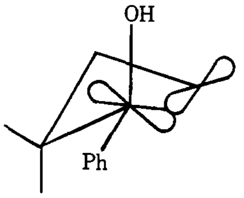
[28] Estimated quantum yield for product formation from the 1,4-biradical intermediate.

[29] (a) A. Padwa, E. Alexander, and M. Niemcyzk, *J. Amer. Chem. Soc.*, **91**, 456 (1969); (b) R. B. Gagosian, J. C. Dalton, and N. J. Turro, *ibid.*, **92**, 4752 (1970).

[30] (a) D. S. Weiss, N. J. Turro, and J. C. Dalton, *Mol. Photochem.*, **2**, 91 (1970); (b) N. Sugiyama, K. Yamada, and H. Aoyama, *J. Chem. Soc. C*, 830 (1971), and references therein.

[31] J. B. Lambert and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 3384, 3891 (1965).

[32] (a) F. Lautenschlaeger and G. F. Wright, *Can. J. Chem.*, **41**, 863 (1963); (b) E. Adman and T. N. Margulis, *Chem. Commun.*, 641 (1967); (c) *J. Amer. Chem. Soc.*, **90**, 4517 (1968).



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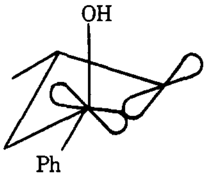

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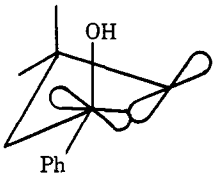

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ence of a 1,3-diaxial interaction in the transition state for cyclobutanol formation. Since γ substituents alone do not give rise to large nonbonded interactions in either the elimination or cyclization transition states it is not surprising that the quantum yields for elimination and cyclization products do not change substantially in going from **1** to **4** to **9**.

Further evidence for the importance of steric interactions on behavior of the 1,4-biradical intermediates is provided by the stereoselectivity of the cyclization reaction. The stereochemical assignments given in Table I are based primarily on the nmr chemical shifts of the methyl protons. Methyl protons cis to the phenyl group are shielded by aromatic ring current and appear at $\sim$0.5 ppm higher field than the trans methyl protons. The only exceptions to this generalization are the methyl doublets in the cyclization products of **6** which have chemical shifts intermediate between those for the other cis and trans methyl protons. This may indicate a somewhat different conformation for the cyclobutanols from **6** compared to those from the other ketones. Both **2** and **4** form 2-methyl-1-phenylcyclobutanol; however, whereas a 3:1 trans:cis ratio is observed for **4**, only the trans isomer (>95%) is observed for **2**. The high stereoselectivity of **2** may be due to a repulsive interaction of the phenyl and α-methyl groups in the 1,4 biradical. The interaction between the phenyl and γ-methyl groups in the biradical from **4** should be small until the 1,4 bond is almost completely formed. The 3:1 trans,trans to trans,cis ratio observed for **5** can be interpreted as a superposition of the α methyl being all trans as in **2** and the γ methyl being 3:1 trans:cis as in **4**. No cis,cis isomer was detected. The smaller trans:cis ratio for **6** (1.4:1) probably reflects greater steric crowding in the transition state for cyclization.

In summary, the effects of methyl substituents on the behavior of 1,4-biradical intermediates can be explained in terms of the biradical conformations required for cyclization and elimination. Steric interactions which increase the energy of either conformation will result in a lowered quantum yield for product formation and an increase in the quantum yield for return of the biradical to the ground state ketone. These steric interactions need be no larger than $\sim$1 kcal/mol to account for the observed changes in product ratios and quantum yields. Since α, β, and γ substituents introduce different steric interactions into the transition state for cyclization and elimination, some degree of control over product composition and stereochemistry may be attained by the proper choice of substituents. Striking evidence for this has been provided by the effect of α substituents on the photochemistry of cycloalkyl and bicycloalkyl phenyl ketones.[8,25]

Experimental Section

Preparation of Ketones. Ketones **2**, **3**, **7**, **8**, and **9** were synthesized from the corresponding alkyl halide and benzonitrile or benzaldehyde using standard Grignard reactions. Ketones **3** and **6** were prepared from **1** and **4** (Eastman) by dialkylation with sodium hydride and methyl iodide. Reaction of 3,3-dimethylacrylic acid (Aldrich) with phenyllithium followed by conjugate addition of 2-propylmagnesium bromide in the presence of cuprous ion[33] afforded ketone **10**. All ketones were purified by column chromatography on silica gel or by preparative vpc (5 ft × 0.25 in. 20% FFAP on Chromosorb W) and had ir, nmr, and uv spectra consistent with the assigned structures. Infrared spectra were recorded on a Beckman IR 10 spectrophotometer, nmr spectra on a Varian A-60 or T-60 spectrometer in CCl_4 solution, ultraviolet spectra on a Cary 14 spectrophotometer in *n*-hexane solution, and emission spectra on a Perkin-Elmer MPF-2A with phosphorescence attachment in an ether–isopentane–ethanol (EPA) glass.

Identification of Photoproducts. Benzene solutions containing 1% ketone were photolyzed with a 450-W Hanovia medium-pressure mercury vapor lamp through Pyrex to about 50% conversion. Preparative vpc on a 5 ft × 0.25 in. column of 20% FFAP on Chromosorb W or column chromatography on silica gel was used to collect samples of photoelimination and cyclization products. Aryl ketone elimination products were identical with authentic samples. The cyclobutanols were identified by their ir and nmr spectra in CCl_4 or $CDCl_3$ solution (Table I). The nmr spectra of the cyclobutanols from **6** were also recorded with added $Eu(DPM)_3$ (Alfa Inorganics). Alkane and alkene products from the α-cleavage reactions of **3** and **6** were identified by vpc coinjection with authentic samples (Phillips or Chemical Samples Co.) on a 20 ft × $^1/_8$ in. column of 20% Carbowax on Chromosorb P.

Quantum Yields. Solutions 0.05 *M* in ketone and 0.002 *M* in tetradecane internal standard were degassed and sealed under vacuum in 13-mm o.d. Pyrex tubes. The tubes were photolyzed to <5% conversion on a merry-go-round apparatus at 25 ± 2° using a Hanovia 450-W lamp and a potassium chromate filter solution to isolate the 313-nm irradiation. Photolyzed solutions were analyzed for product formation on a Hewlett-Packard 5750 dual flame gas chromatograph with a calibrated 5 ft × $^1/_8$ in. column of 4% QF 1 and 1% Carbowax 20M on Chromosorb G. Benzophenone–benzhydrol actinometer solutions[11] were photolyzed simultaneously and analyzed at 360 nm using a Beckman DU spectrophotometer with Gilford attachment Model 222. Reported quantum yields are the result of multiple vpc analyses of two or more solutions, overall accuracy ±5%. Light intensities were approximately 5×10^{-6} einstein $l.^{-1}$ sec^{-1}. The solvent was spectro grade benzene (Fisher) further purified by distillation from phosphorus pentoxide.

Quenching Studies. Varying amounts of *trans*-piperylene (Chemical Samples Co.) were added to ketone solutions which otherwise were prepared, irradiated, and analyzed as for quantum yield determination. Quenching studies with naphthalene (zone refined) were carried out on 0.1 *M* ketone solutions using Corning 7-54 and 0-52 filters to isolate 366-nm irradiation.

Intersystem crossing quantum yields were determined by the method of Lamola and Hammond[14] as previously described.[7]

Acknowledgment. The authors thank P. J. Wagner for stimulating discussions and the exchange of unpublished results.

Appendix

The enthalpies of reaction given in Table V were estimated using Benson's[23] group additivity data to calculate heats of formation ($\Delta H_f°$) and literature values for bond dissociation energies and heats of formation of free radicals. The heat of formation of pivalo-

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(33) J. A. Marshall and N. H. Anderson, *J. Org. Chem.*, **31**, 667 (1966).

phenone (**11**) is calculated directly from group additivity data as shown in eq 7. Using literature values for the

$$\Delta H_f^\circ = 5\Delta H_f^\circ(\mathrm{C_B{-}H}) + \Delta H_f^\circ(\mathrm{C_B{-}CO}) + \Delta H_f^\circ(\mathrm{CO{-}C_B,C}) + \Delta H_f^\circ(\mathrm{C{-}CO,C_3}) + 3\Delta H_f^\circ(\mathrm{C{-}C,H_3}) = 16.5 + 9.7 - 37.6 + 1.6 - 30.2 = -40.0 \text{ kcal/mol} \tag{7}$$

heats of formation of benzoyl[22b] and *tert*-butyl[23] radicals, the heat of reaction for α-cleavage is obtained (eq 8). Similarly, the heats of reaction for α-cleavage

$$\Delta H_r^\circ = DH^\circ(\mathrm{PhCO{-\!\!-}C(CH_3)_3}) = \Delta H_f^\circ(\mathrm{Ph\dot{C}O}) + \Delta H_f^\circ(\mathrm{\dot{C}(CH_3)_3}) - \Delta H_f^\circ(\mathrm{PhCOC(CH_3)_3}) = 26.1 + 6.7 - (-40.0) = 72.8 \text{ kcal/mol} \tag{8}$$

of α-methylbutyrophenone (**2**) and butyrophenone (**1**) are calculated to be 77 and 79 kcal/mol, respectively. At least two serious difficulties arise in interpreting these calculations. First, the calculations are for standard states of ideal gases. Assumption of equal heats of solution for product and reactant is hazardous but necessary. Second, steric correction terms have been neglected. A strain energy of ~3 kcal/mol for pivalophenone can be estimated from the thermochemical data of Colomina.[34] Correction for strain would lower the calculated heat of reaction to ~70 kcal/mol.

The method for estimating heats of reaction for γ-hydrogen abstraction (eq 9) has been previously out-

$$\Delta H_r^\circ = \Delta H_f^\circ(\mathrm{Ph\dot{C}OHCH_2CH_2\dot{C}H_2}) - \Delta H_f^\circ(\mathrm{PhCOCH_2CH_2CH_3}) \tag{9}$$

lined.[6] Heats of formation for butyrophenone (eq 10) and its carbinol (eq 11) are calculated from group

$$\Delta H_f^\circ(\mathrm{PhCOCH_2CH_2CH_3}) = 5\Delta H_f^\circ(\mathrm{C_B{-}H}) + \Delta H_f^\circ(\mathrm{C_B{-}CO}) + \Delta H_f^\circ(\mathrm{CO{-}C_B,C}) + \Delta H_f^\circ(\mathrm{C{-}CO,C,H_2}) + \Delta H_f^\circ(\mathrm{C{-}C_2,H_2}) + \Delta H_f^\circ(\mathrm{C{-}C,H_3}) = 16.5 + 9.7 - 37.6 - 5.0 - 5.0 - 10.1 = -31.5 \tag{10}$$

$$\Delta H_f^\circ(\mathrm{PhCHOHCH_2CH_2CH_3}) = 5\Delta H_f^\circ(\mathrm{C_B{-}H}) + \Delta H_f^\circ(\mathrm{C_B{-}C}) + \Delta H_f^\circ(\mathrm{C{-}C_B,C,O,H}) + \Delta H_f^\circ(\mathrm{O{-}C,H}) + 2\Delta H_f^\circ(\mathrm{C{-}C_2,H_2}) + \Delta H_f^\circ(\mathrm{C{-}C,H_3}) = 16.5 + 5.5 - 7.0 - 37.9 - 9.9 - 10.1 = -32.9 \tag{11}$$

additivity data. Assuming a bond dissociation energy for the benzyl C–H bond similar to that for a cumyl C–H bond,[35] the 1,4-biradical heat of formation can be calculated (eq 12). Using the results from eq 10 and

$$\Delta H_f^\circ(\mathrm{Ph\dot{C}OHCH_2CH_2\dot{C}H_2}) = DH^\circ(\mathrm{PhCOHR{-\!\!-}H}) + DH^\circ(\mathrm{PhCOCH_2CH_2CH_2{-\!\!-}H}) + \Delta H_f^\circ(\mathrm{PhCHOHCH_2CH_2CH_3}) - 2\Delta H_f^\circ(\mathrm{H\cdot}) = 74 + 98 - 32.9 + (-104.2) = 34.9 \text{ kcal/mol} \tag{12}$$

12 in eq 9, $\Delta H_r^\circ = 66.4$. Similarly, the heats of reaction for γ-hydrogen abstraction for valerophenone (**4**) and γ-methylvalerophenone (**9**) are calculated to be 64 and 60 kcal/mol, respectively. In view of the similar gross structure of reactant ketone and product biradical, assumption of equal heats of solution and neglect of steric correction terms is less unreasonable than is the case for the α-cleavage reactions. Enthalpies of reaction for dialkyl ketones were calculated in an analogous manner.

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(34) M. Colomina, C. Latorre, and R. Perez-Ossorio, *Pure Appl. Chem.*, **2**, 133 (1961).

(35) P. Gray and A. Williams, *Chem. Rev.*, **59**, 239 (1959)