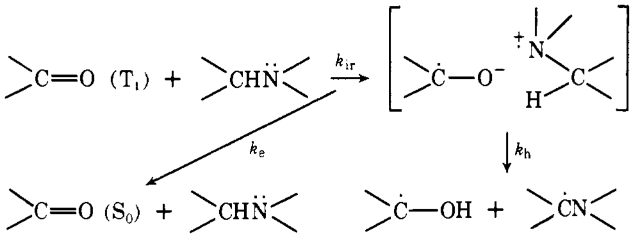
Effects of Concentration of Amine and of Medium in Photoreduction of Ketones by Amines

Abraham H. Parola, Anita W. Rose, and Saul G. Cohen*

Contribution from the Department of Chemistry, Brandeis University, Waltham, Massachusetts 02154. *Received January 23, 1975*

Abstract: Quantum yields have been determined for photoreduction, over wide ranges of amine concentration (0.005–4.5 M) of benzophenone by cyclohexylamine (a) in benzene and (b) in *tert*-butyl alcohol and of 4-benzoylbenzoate (c) by triethylamine and (d) by 2-butylamine in 1:1 water-pyridine at pH 12. At low concentrations of amine (<0.02 M), in a and b, linear plots of φ^{-1} vs. (amine)$^{-1}$ are obtained, leading to low, useful, values of k_d/k_{ir}, 0.0012 M, and to low extrapolated values of φ_{lim}, 0.60 and 0.79, respectively. At high concentrations of amine, values of φ are higher, and the plots are curved, leading to values of φ_{lim}, 1.09 and 1.49, respectively, and to high apparent values of k_d/k_{ir}. Inhibition by piperylene of photoreduction by high concentration of amine leads, in system a, to $k_{ir} = 3.7 \times 10^8$ M^{-1} sec^{-1}, similar to the value determined by quenching of phosphorescence, and $k_d = 4.5 \times 10^5$ sec^{-1}; in system b, it leads to $k_{ir} = 1.4 \times 10^8$ M^{-1} sec^{-1} and to $k_d = 1.7 \times 10^5$ sec^{-1}, compared with 1.1×10^5 sec^{-1} observed by decay of phosphorescence. System c shows a smaller enhancement of quantum yield by high concentration of amine; $k_{ir} = 8.5 \times 10^8$ M^{-1} sec^{-1} at both 1 and 0.02 M triethylamine, determined by naphthalene quenching. Increased quantum yield at high amine concentration may arise from excitation of ground-state ketone–amine complex, charge-transfer interaction of this with amine in solution, and catalysis by the initial amine of the proton transfer from the radical cation to the radical anion in the charge-transfer complex. Equilibrium constants for ground-state benzophenone–cyclohexylamine complex are estimated to be 8 ± 2 M^{-1} in benzene, 3 ± 1 M^{-1} in *tert*-butyl alcohol. This effect is less important when the aqueous pyridine may assist the transfer and, in system d, a linear plot of φ^{-1} vs. (amine)$^{-1}$ is observed over the entire concentration range. Kinetic expressions are developed.

It has been proposed[1,2] that photoreduction of aromatic ketones by amines proceeds via rapid formation of a charge-transfer complex (CTC) rate constant k_{ir}. Then, either hydrogen transfer and formation of radicals (k_h) or spin inversion, charge destruction, and quenching (k_e) occurs (eq 1).



(1)

The quantum yield for photoreduction is strongly affected by the relative importance of k_h and k_e, i.e., by the fraction, $f = k_h/(k_h + k_e)$. The dependence of quantum yield on concentration of amine (AH$_2$) and of added quencher (Q) is indicated in eq 2.[3,4] This differs from the equation for photoreduction by an alcohol[5] by the factor f.

$$1/\varphi = 1/af + k_d/afk_{ir}(\mathrm{AH_2}) + k_q(\mathrm{Q})/afk_{ir}(\mathrm{AH_2}) \quad (2)$$

A plot of φ^{-1} vs. (AH$_2$)$^{-1}$, in the absence of quencher, should be linear, intercept = $1/af$, slope = k_d/afk_{ir}, and ratio of slope to intercept = k_d/k_{ir}, where k_d is the unimolecular decay constant for the excited ketone in the medium. A plot of φ^{-1} vs. (Q) at constant concentration of amine should be linear, with slope = $k_q/afk_{ir}(\mathrm{AH_2})$, intercept = $[k_d + k_{ir}(\mathrm{AH_2})]/afk_{ir}(\mathrm{AH_2})$, and ratio of slope to intercept = $k_q/[k_d + k_{ir}(\mathrm{AH_2})]$, in which k_q may be the rate constant for diffusion-controlled quenching. In this way, k_{ir} and k_d may be evaluated. Values of k_{ir} and k_d may also be determined more directly, k_{ir} by quenching of phosphorescence[7] of the triplet ketone by the amine,[8] and k_d from decay of triplet absorption[9] or emission[7] in flash photolysis studies.

The linear relationship between φ^{-1} and (AH$_2$)$^{-1}$ is frequently not observed at high concentration of reducing agent. In photoreduction of benzophenone by 2-propanol in benzene, quantum yields decreased at concentrations of alcohol higher than 1 M. This was attributed to greater formation of light-absorbing transients, which may also act as quenchers, in the more hydroxylic medium.[10] In photoreduction of fluorenone[11-14] and p-aminobenzophenone[1] by triethylamine in hydrocarbon medium, quantum yields decreased when concentrations of amine were greater than 0.1 and 1.0 M, respectively. Light-absorbing transients were not present, and the effect was attributed to low efficiency of formation of reactive triplets in polar solvents and at high amine concentrations.

Photoreduction of benzophenone by primary amines in benzene appeared not to be complicated, and kinetic analysis was made in accord with eq 2.[2] However, light-absorbing transients prevented kinetic analysis in photoreduction of benzophenone by secondary and tertiary amines in benzene.[2] This effect decreased almost completely in 1:1 water-pyridine at pH 12, and kinetic analysis was made of photoreduction by the three classes of amines.[3] However, anomalies were observed in the kinetic constants which were obtained. In the photoreduction of benzophenone by 0.1–1.0 M 2-butylamine in benzene,[2,3] a value of $k_d/k_{ir} = 0.03$ M was obtained, indicating $k_{ir} = 3\text{–}5 \times 10^6$ M^{-1} sec^{-1} based on $k_d = 1 \times 10^5$ sec^{-1} determined by decay of triplet absorption,[9] or 1.5×10^5 sec^{-1}, determined by decay of benzophenone phosphorescence.[7] However, quenching of this photoreduction by naphthalene led to $k_q/k_{ir} = 28$, and $k_{ir} = 2 \times 10^8$ M^{-1} sec^{-1} based on $k_q = 6.3 \times 10^9$ M^{-1} sec^{-1}.[13] Quenching of phosphorescence of benzophenone by the amine led to $k_{ir} = 2.5 \times 10^8$ M^{-1} sec^{-1},[8] supporting the value of k_{ir}. This value of k_{ir} would lead to a high value of $k_d = 7 \times 10^6$ sec^{-1} if one accepted the k_d/k_{ir} ratio obtained by variation in concentration of amine. Variation of concentration of amine in benzene appeared to lead to much too high a value of k_d/k_{ir}, to incorrectly high value of k_d if reasonable values of k_{ir} are accepted, and to incorrectly low value of k_{ir} if reasonable values of k_d are accepted.

In the photoreduction of benzophenone by 0.05–1.0 M 2-butylamine in water-pyridine at pH 12,[3] k_d/k_{ir} again had a value of 0.031 M. However, k_{ir} had a lower value than in benzene, as hydrogen bonding of water to the n electrons of the amine decreased the rate of attack of the triplet,[3] and a reasonable value of k_d resulted in this medium. The values of $k_q/k_{ir} = 170$, $k_q = 3 \times 10^9\ M^{-1}\ \text{sec}^{-1}$ led to $k_{ir} = 1.8 \times 10^7\ M^{-1}\ \text{sec}^{-1}$ and $k_d = 5.5 \times 10^5\ \text{sec}^{-1}$. Also, in the photoreduction of benzophenone by 2-propanol in benzene and in 1:1 water-pyridine, values of k_d determined by variations in concentration of 2-propanol and naphthalene were 2.7×10^5 and $1.5 \times 10^5\ \text{sec}^{-1}$, respectively,[3] close to the directly determined values. In the photoreduction of 4-benzoylbenzoate anion in 1:1 water-pyridine, pH 12, values of k_d, determined by variations in concentrations of reducing agent and quencher naphthalene, showed small variations;[3] with 2-propanol as reducing agent, $k_d = 2.8 \times 10^6\ \text{sec}^{-1}$; with 2-butylamine, $k_d = 6.3 \times 10^6\ \text{sec}^{-1}$; with *N*-methyl-2-butylamine, $k_d = 4.8 \times 10^6\ \text{sec}^{-1}$; with *N*,*N*-dimethyl-2-butylamine, $k_d = 1.0 \times 10^7\ \text{sec}^{-1}$; with triethylamine, $k_d = 1.3 \times 10^7\ \text{sec}^{-1}$.

The results indicated that Stern-Volmer kinetics may lead to correct kinetic constants in photoreduction by alcohols. In photoreduction by amines, effects of quenchers may lead to satisfactory values of k_{ir}, but variation in concentration of amine would not lead to useful values of k_d, particularly in hydrocarbon medium. The reasons for this have now been sought in studies over a wide range of amine concentrations, 0.005-5.0 *M*, of some systems which are not complicated by light-absorbing transients or variations in triplet yield.

Experimental Section

Materials. Argon (Airco Welding grade) was passed through Drierite. Benzene (Eastman Spectrograde) was distilled, bp 80°, and a center cut was used. *tert*-Butyl alcohol (Matheson Coleman and Bell) was distilled under N_2, bp 82°. Pyridine (Fisher Certified ACS) was distilled, bp 115°. Benzophenone (Fisher Certified Reagent), mp 47.5-48.5°, and 4-benzoylbenzoic acid (Aldrich), mp 202-202.5°, were used. 2-Butylamine (Eastman) was distilled directly before use, bp 63-64°. Cyclohexylamine (Eastman) was distilled, bp 70° (75 mm), and stored under N_2 in a refrigerator. Triethylamine (Eastman) was distilled under N_2 directly before use, bp 88-89°. Naphthalene (Fisher Certified Reagent) was used as received. Piperylene (Aldrich) was distilled, bp 42° C.

Irradiation. Calibrated Pyrex tubes, 1 × 1 × ~10 cm, sealed to Fisher-Porter Teflon valves, containing 3-4 ml aliquots, were degassed by two freeze-pump-thaw cycles, cooled in Dry Ice-acetone, evacuated to 0.05-0.1 mm Hg, and left under argon. For monochromatic light, an Osram SP-200 mercury vapor point source was used. For irradiations on the wheel, an 85-W/G.E. H85-A3 medium-pressure mercury lamp was used. With Pyrex filtering, ~95% of the absorption by benzophenone is at 366 nm. The irradiation wheel and method of analysis of nonopaque solution were described previously.[15,16]

Solutions of benzophenone and varying concentrations of cyclohexylamine in benzene were irradiated on a Bausch and Lomb 38-86-01 monochromator at 334 and 366 nm in 1-cm square tubes to which 1-mm cells were attached. Rates of reduction were determined from the absorbance at 344 nm measured in the 1-mm cell or, for the more dilute solutions, directly in the 1-cm cell. Quantum yields were determined by comparison with the rates of reduction of 0.06 *M* benzophenone by 2-butylamine, $\varphi = 1.13$,[2] irradiated alternately.

Solutions of benzophenone and varying concentrations of cyclohexylamine in *tert*-butyl alcohol were irradiated in Pyrex simultaneously on the wheel. Rates were determined from the decrease in absorbance at 335 nm by least-squares treatment of slopes of plots of OD vs. time. Rates were converted to quantum yields by comparison with the rate of photoreduction by 1 *M* cyclohexylamine in benzene irradiated simultaneously; $\varphi = 1.04$, determined above. The rate of photoreduction by 1.0 *M* cyclohexylamine in *tert*-butyl alcohol was 1.31 times that in benzene.

Table I. Quantum Yields. Photoreduction of Benzophenone by Cyclohexylamine in Benzene

Run	[Ketone], *M*	[Amine], *M*	$\varphi_{334\text{nm}}$	$\varphi_{366\text{nm}}$
1	0.060	1.00	1.04	
2	0.060	0.200	0.85	
3	0.060	0.106	0.77	
4	0.060	0.0500	0.71	
5	0.0060	0.0302	0.59	
6	0.0060	0.0204		0.56
7	0.0060	0.0097	0.54	0.53
8	0.0060	0.0051		0.49
9	0.0060	0.0049	0.47	

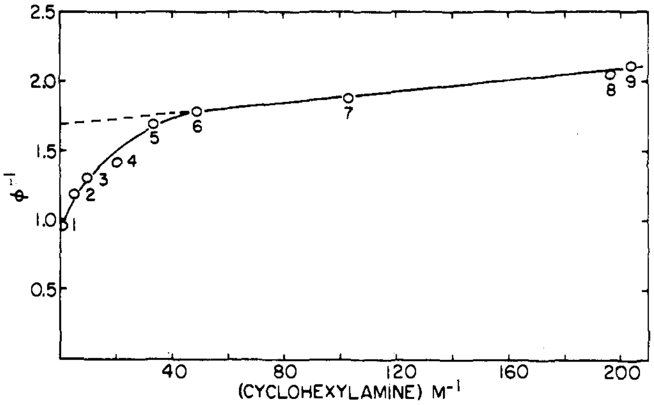


Figure 1. Photoreduction of benzophenone by cyclohexylamine in benzene. Effect of amine concentration. Numbers refer to data in Table 1.

Solutions of 4-benzoylbenzoate and varying concentrations of triethylamine in 1:1 water-pyridine, pH 12, were irradiated in Pyrex simultaneously on the wheel. Rates were determined from the decrease in absorbance at 334 nm. Rates were converted to quantum yields by comparison with the rate of the 1 *M* amine solution for which the quantum yield, 0.68, had been determined previously[3] by ferrioxalate actinometry. Photoreduction of 2-butylamine in this medium was followed similarly. The quantum yield at 1.0 *M* amine had been determined previously, 0.50.[3]

Rates of photoreduction in the presence of quencher were followed as described for experiments in the absence of quencher. Solutions with varying concentrations of quencher, and the solution without quencher, at the same concentration of amine, were irradiated simultaneously on the wheel.

Phosphorescence Studies. Phosphorescence quenching was examined on a Farrand spectrofluorimeter. Solutions of benzophenone, ~0.02 *M*, and varying concentrations of cyclohexylamine, $<10^{-3}$ *M*, in benzene were degassed and irradiated at 380 nm under argon. Emission intensities were monitored at 450 nm and compared with the intensity in the absence of amine. The baseline was determined from the residual intensity in the presence of a large quantity of amine.

The lifetime of benzophenone triplet in *tert*-butyl alcohol was determined in the photoflash equipment of Professor C. Steel, by measurement of the exponential decay in vacuum of the triplet phosphorescence[7] of a 3-ml aliquot of 0.01 *M* benzophenone in *tert*-butyl alcohol evacuated to 4×10^{-2} mmHg.

Results

Photoreduction of benzophenone by cyclohexylamine in benzene was carried out on a monochromator, and results are summarized in Table I and Figure 1.

The results at higher amine concentrations, runs 1-5, lend themselves poorly to a linear plot of φ^{-1} vs. $(AH_2)^{-1}$, slope ~0.03, intercept = 0.92, and limiting quantum yield = 1.09, and ratio of slope to intercept, apparent k_d/k_{ir} = 0.03 *M*. The results at the lower concentrations, runs 5-9, may be converted to a satisfactory linear plot, which has quite different properties, slope = 0.0020 *M*, intercept = 1.67, limiting quantum yield = 0.60, and ratio of slope to intercept k_d/k_{ir} = 0.0012 *M*. Over the wide range of concentrations, 0.005-1.0 *M*, the plot shows distinct curvature (Figure 1) with an apparent higher order dependence of

Table II. Quantum Yields. Photoreduction of 0.008 *M* Benzophenone by Cyclohexylamine in *tert*-Butyl Alcohol

Run	[Amine], *M*	Quantum yield (φ)
1	4.5	1.48
2	3.0	1.36
3	1.0	1.36
4	0.5	1.21
5	0.09	0.91
6	0.05	0.80
7	0.02	0.83
8	0.01	0.67
9	0.008	0.67
10	0.006	0.67

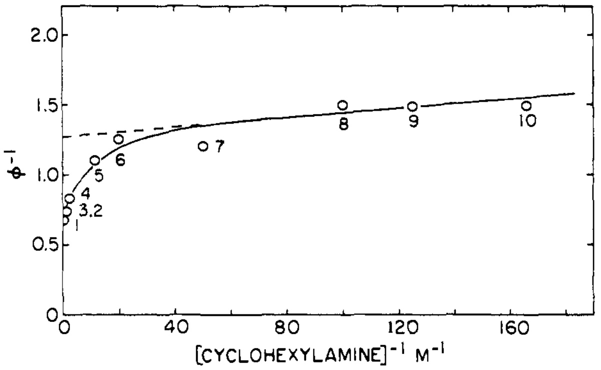


Figure 2. Photoreduction of 0.008 *M* benzophenone by cyclohexylamine in *tert*-butyl alcohol. Effect of amine concentration. Numbers refer to data in Table II.

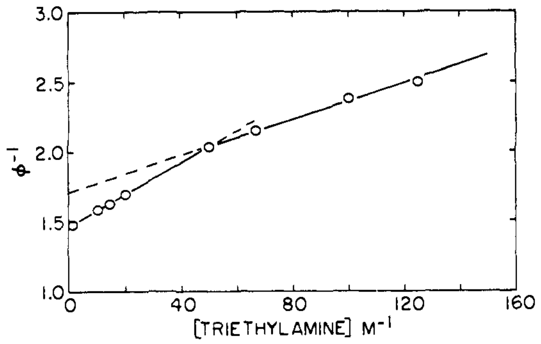


Figure 3. Photoreduction of 0.008 *M* 4-benzoylbenzoate by TEA in 1:1 (v/v) water-pyridine at pH ~12.

Table III. Photoreduction by Triethylamine and by 2-Butylamine of 0.008 *M* 4-Benzoylbenzoate in 1:1 Water–Pyridine at pH 12. Quantum Yields (φ)

[Amine], *M*	φ Triethylamine	φ 2-Butylamine
2.0		0.57
1.0	0.68	0.50
0.1	0.63	0.27
0.07	0.62	0.23
0.05	0.59	0.17
0.02	0.49	0.09
0.015	0.46	0.059
0.01	0.42	0.046
0.008	0.40	0.036

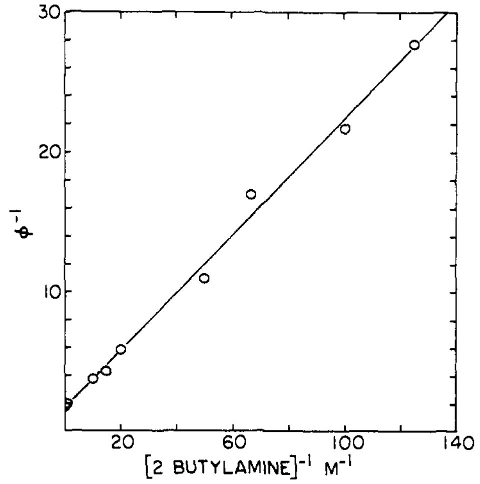


Figure 4. Photoreduction of 0.008 *M* benzoylbenzoate by 2-butylamine in 1:1 water-pyridine (v/v) at pH ~12.

quantum yield on concentration of amine at higher than at low amine concentration. The value of k_d/k_{ir} at low concentrations of amine, and the measured value of k_d,[7] 1.5×10^5 sec^{-1}, lead to $k_{ir} = 1.2 \times 10^8$ M^{-1} sec^{-1}, similar to values for interaction with 2-butylamine determined by phosphorescence quenching and by naphthalene quenching of photoreduction.[2]

Photoreduction of 0.008 *M* benzophenone by 0.006-4.5 *M* cyclohexylamine was then studied in *tert*-butyl alcohol. In the presence of 3 *M* cyclohexylamine λ_{max} was at 3380 Å as compared with 3330 Å in 0.09 *M* amine in *tert*-butyl alcohol and 3400 Å in benzene. The uv spectra indicated formation of very little absorbing transient. Results are summarized in Table II and Figure 2.

Again curvature is seen in the plot of φ^{-1} vs. $(AH_2)^{-1}$ over the whole concentration range, with a greater increase in quantum yield at the higher concentrations. The data at high concentrations do not lend themselves well to a linear inverse plot; they indicate an intercept of 0.67 and limiting quantum yield of 1.49, slope of ~0.03 *M*, and ratio of slope to intercept, apparent k_d/k_{ir} ~0.04 *M*; data at low concentrations, 0.006-0.05 *M*, lead to slope 0.0017 *M*, intercept = 1.27, and limiting quantum yield = 0.79, and ratio of slope to intercept, $k_d/k_{ir} = 0.0013$ *M*.

A value of k_d for benzophenone triplet in *tert*-butyl alcohol was obtained by study of the decay of phosphorescence. Values of emission intensities at the indicated times after flash were: 5 μsec, 4.55; 10 μsec, 2.53; 15 μsec, 1.49; 20 μsec; 0.86; 25 μsec, 0.53. A linear plot of log *I* vs. *t* was obtained, slope -4.8×10^4 sec^{-1}. From the expression $I = I_0e^{-t/\tau}$ and slope = 0.434 k_d, $k_d = 1.1 \times 10^5$ sec^{-1}. From the value of $k_d/k_{ir} = 0.0013$ *M*, $k_{ir} = 8.5 \times 10^7$ M^{-1} sec^{-1}.

Similar studies were carried out on the photoreduction of 0.008 *M* 4-benzoylbenzoate in 1:1 v/v water-pyridine at pH 12 with varying concentrations of triethylamine and 2-butylamine. Results are summarized in Table III and in Figures 3 and 4.

The plot for triethylamine shows slight curvature and a small increased effect of concentration at high concentration of amine. Least-squares analysis of the data at higher concentration, >0.02 *M*, leads to slope = 0.0114 *M*, intercept = 1.46, and limiting quantum yield = 0.68, and ratio of slope to intercept, apparent $k_d/k_{ir} = 0.0078$ *M*. The data over the low concentration range, 0.008-0.02 *M* lead to slope = 0.0061 *M*, intercept = 1.75, and limiting quantum yield 0.57, and ratio $k_d/k_{ir} = 0.0035$ *M*; correlation factors are 0.995 and 0.996. The plot of data for photoreduction by 2-butylamine shows no curvature over the entire range of concentration, and the system behaves in accord with eq 2,

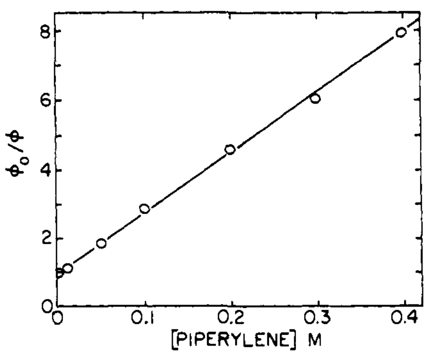


Figure 5. Photoreduction of 0.008 *M* benzophenone by 1 *M* cyclohexylamine in benzene in the presence of piperylene.

slope = 0.21 *M*, intercept = 1.64, ratio k_d/k_{ir} = 0.13 *M*, and limiting quantum yield = 0.61.

To gain information about the nature of the more efficient reductions at high amine concentrations, effects of known triplet quenchers were examined. Photoreduction of 0.008 *M* benzophenone by 1 *M* cyclohexylamine in benzene was studied in the presence of 0-0.4 *M* piperylene. A linear plot of φ_0/φ vs. concentration of quencher was obtained to the extent examined, to over 85% quenching (Figure 5). Least-squares analysis led to intercept = 1.016 ± 0.052, slope = 17.17 ± 0.25 M^{-1}, and correlation factor = 0.998. The ratio of slope to intercept, $k_q/[k_d + k_{ir}(\mathrm{RH})]$ = 17 M^{-1}, k_q/k_{ir} = 17, k_{ir} = 3.7 × 10^8 M^{-1} sec^{-1} based on k_q = 6.3 × 10^9 M^{-1} sec^{-1}. The value of k_{ir} for reaction of benzophenone triplet with cyclohexylamine in benzene was also determined by measurement of quenching of phosphorescence of ~0.02 *M* benzophenone in this system. Values of I_0/I, the ratio of phosphorescence intensity in the absence and presence of amine, are as follows (the first number in each pair being the amine concentration, the second, I_0/I): 0.195 m*M*, 1.42; 0.300 m*M*, 1.56; 0.390 m*M*, 1.78; 0.585 m*M*, 2.19; 0.780 m*M*, 2.54. The value of k_{ir} was obtained from a least-squares calculation of the slope of the plot of I_0/I vs. concentration of amine (eq 3).

$$I_0/I = 1 + \tau_0 k_{ir}(\mathrm{Am}) \qquad (3)$$

From the slope, 0.0020 M^{-1}, and τ_0 = 6.5 × 10^{-6} sec,[7] k_{ir} = 3.1 × 10^8 M^{-1} sec^{-1}.

Photoreduction of 0.008 *M* benzophenone by 1 *M* cyclohexylamine in *tert*-butyl alcohol was studied in the presence of 0-0.2 *M* piperylene, and >85% quenching was observed (Figure 6). Least-squares analysis led to intercept 1.07 ± 0.08, slope 38.4 ± 0.9 M^{-1}, correlation factor 0.996. The ratio of slope to intercept, $k_q/[k_d + k_{ir}(\mathrm{RH})]$ = 36 M^{-1}, k_q/k_{ir} = 37, k_{ir} = 1.3 × 10^8 M^{-1} sec^{-1} based on k_q = 5 × 10^9 M^{-1} sec^{-1}.

Photoreduction of 0.008 *M* 4-benzoylbenzoate by 1 *M* triethylamine in 1:1 water-pyridine at pH 12 was examined in the presence of 0.01-0.20 *M* naphthalene. Data are summarized in Table IV. Values of k_{ir} for tertiary amines are within a factor of 3 of diffusion-controlled rates, and physical quenchers lead to small effects compared with those in systems with lower values of k_{ir}. At 0.20 *M* naphthalene and 1.0 *M* amine, the rate was decreased by 32%; linear least-squares treatment of φ_0/φ vs. [Q] led to an intercept of 0.984 ± 0.005, slope 2.83 ± 0.07, and correlation factor 0.996; ratio of slope to intercept $k_q/[k_d + k_{ir}(\mathrm{RH})]$ = 2.9, k_q/k_{ir} = 2.9, k_{ir} = 8.6 × 10^8 M^{-1} sec^{-1}, based on k_q = 2.5 × 10^9 M^{-1} sec^{-1}.[3] Effects of naphthalene on reduction by 0.02 *M* triethylamine were greater; 0.04 *M* quencher decreased the quantum yield to 0.1 from 0.48 in its absence. Least-squares treatment of the data in Table IV led to a ratio of slope to intercept of 124.5 and correlation factor 0.985. In another similar run, this ratio was 127.8 and the correlation factor 0.987. The average value, 126.1, leads to k_q/k_{ir} = 3.0, k_{ir} = 8.3 × 10^8 M^{-1} sec^{-1}, the same as at higher concentration of amine.

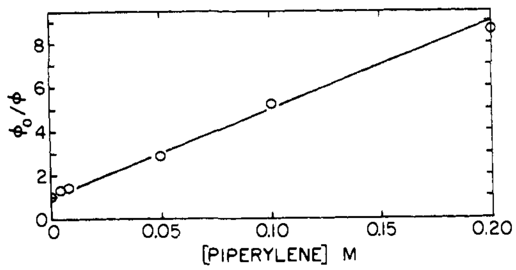


Figure 6. Photoreduction of 0.008 *M* benzophenone by 1 *M* cyclohexylamine in *tert*-butyl alcohol in the presence of piperylene.

Table IV. Photoreduction of 0.008 *M* 4-Benzoylbenzoate in 1:1 Water–Pyridine, pH 12, by 1.0 and 0.02 *M* Triethylamine (TEA). Effects of Naphthalene

[Naphthalene], *M*	φ	
	1 *M* TEA	0.02 *M* TEA
0	0.68	0.48
0.005		0.35
0.008		0.32
0.010	0.67	0.28
0.015		0.22
0.02		0.17
0.03	0.64	0.14
0.04		0.10
0.05	0.60	
0.10	0.48	
0.20	0.44	

Data for photoreduction at high and low concentration ranges of amines are summarized in Table V. Except in photoreduction by 2-butylamine in the aqueous system, higher quantum yields are observed at high amine concentration than are indicated by extrapolation of the results at low concentration. This is reflected in higher apparent values of the k_d/k_{ir} ratios at high amine concentration. Values obtained for k_{ir} are less dependent on the range of concentration of amine, and the high values of k_d/k_{ir} would lead to high apparent values of k_d. The low value of k_d/k_{i} at low concentration of cyclohexylamine in benzene, 0.0012 *M*, multiplied by the value of k_{ir} obtained by piperylene quenching of the high concentration of amine leads to k_d = 4.5 × 10^5 sec^{-1}, within a factor of ~3 of the value determined by quenching of phosphorescence.[7] In *tert*-butyl alcohol k_d/k_{ir} = 0.0013 *M*, k_{ir} = 1.3 × 10^8 M^{-1} sec^{-1}, k_d = 1.7 × 10^5 sec^{-1}, compared with 1.1 × 10^5 sec^{-1} from phosphorescence quenching. In the 4-benzoylbenzoate-triethylamine reaction in water-pyridine, from k_d/k_{ir} = 0.0035 *M* and k_{ir} = 8.3 × 10^8 *M* sec^{-1}, k_d = 2.9 × 10^6 sec^{-1}; this ketone apparently has a lower triplet state lifetime than benzophenone, but it has not been measured directly in this medium. The value may be compared with that for k_d previously reported[3] in photoreduction by 2-butylamine in thi medium, 8.2 × 10^6 sec^{-1}.

Discussion

While it is probably preferable to determine values of k by decay of triplet absorbance or emission, and of k_{ir} b quenching of triplet emission, these methods too are n without problems and often cannot be applied at all. Th photoreduction reactions, leading to free radicals and the products,[5] to dealkylation and deamination of amines

Table V. Photoreduction of Benzophenone (B) and 4-Benzoylbenzoate (4-Bb) at High and Low Concentrations of Cyclohexylamine (c-HA), Triethylamine (TEA), and 2-Butylamine (2-BA)

	Amine							
Ketone	Compd	Concn, M	Solvent	φ_{lim}	k_d/k_{ir}, M[d]	k_q/k_{ir}	k_{ir}, M^{-1} sec^{-1}	k_d, sec^{-1}
B	c-HA	0.03–1.0	C_6H_6	1.09[b]	(0.03)	17	3.7×10^8[e]	(1×10^7)[k]
B	c-HA	0.005–0.02	C_6H_6	0.60[b]	0.0012		3.1×10^8[f]	4.5×10^5[l]
B	c-HA	0.05–4.5	t-C_4H_9OH	1.49[b]	(0.04)	37	1.3×10^8[g]	(5.4×10^6)[k]
B	c-HA	0.006–0.05	t-C_4H_9OH	0.79[b]	0.0013		8.5×10^7[h]	1.7×10^5[m]
4-Bb	TEA	0.02–1.0	1:1 H_2O–C_5H_5N[a]	0.68[c]	(0.0078)	2.9	8.6×10^8[i]	(6.7×10^6)[k]
4-Bb	TEA	0.008–0.02	1:1 H_2O–C_5H_5N[a]	0.57[c]	0.0035	3.0	8.3×10^8[n]	2.9×10^6[n]
4-Bb	2-BA	0.008–2.0	1:1 H_2O–C_5H_5N[a]	0.61[c]	0.13	44	6.3×10^7[j]	8.2×10^6[j]

[a] pH 12. [b] Reduction to pinacol, maximum quantum yield, 2. [c] Reduction to hydrol, maximum quantum yield, 1. [d] Ratio of slope to intercept, φ^{-1} vs. $(\text{Am})^{-1}$; apparent values of k_d/k_{ir}; values in parentheses are anomalous and high. [e] From k_q/k_{ir} (this work), $k_q = 6.3 \times 10^9\ M^{-1}$ sec^{-1}(ref 7). [f] From phosphorescence quenching (this work); $k_{ir} = 1 \times 10^8\ M^{-1}$ sec^{-1} from k_d/k_{ir}, $k_d = 1.5 \times 10^5$ sec^{-1} (ref 7). [g] From k_q/k_{ir}, based on $k_q = 5 \times 10^9\ M^{-1}$ sec^{-1}. [h] From k_d/k_{ir}, $k_d = 1.1 \times 10^5$ sec^{-1} (this work). [i] From k_q/k_{ir} (this work), $k_q = 2.5 \times 10^9\ M^{-1}$ sec^{-1}(ref 3). [j] From reduction studies (ref 3). [k] Values in parentheses are anomalous and high, from high values of k_d/k_{ir}. [l] From k_d/k_{ir} and k_{ir} (this work). [m] From k_d/k_{ir} and k_{ir}, to be compared with 1.1×10^5 sec^{-1} from phosphorescence decay. [n] From k_d/k_{ir} and k_{ir} (footnote i).

show great variations in quantum yield with medium and structure of components and merit detailed kinetic study. When the kinetic constants can be obtained by both the reduction and spectral procedures and compared, additional information may be obtained about the mechanisms of the reduction.

Plots of φ^{-1} vs. $(\text{amine})^{-1}$ over a wide range of amine concentration show downward curvature at high amine concentration in all but one of the photoreductions summarized in Table V and in other similar reductions which we have examined. The deviations from the linearity of eq 2 were less in alkaline aqueous solutions than in organic solvents, and the linear relationship of eq 2 was found in reduction by primary amines in the aqueous system.

In the photoreduction in benzene, a lower concentration of ketone, 0.006 M, was used at low concentrations of amine than at the high concentration of amine, 0.060 M ketone. It is conceivable that part of the decrease in quantum yield at low amine concentration might arise from a lower contribution, at low ketone concentration, of the reaction of amine derived radical with ground state ketone, which leads to the theoretical limiting quantum yield $a = 2$ (eq 4).

$$\text{Ar, Ar}'\text{C}{=}\text{O} + \text{R}\dot{\text{C}}\text{HNH}_2 \rightarrow \text{Ar, Ar}'\dot{\text{C}}\text{OH} + \text{RCH}{=}\text{NH} \quad (4)$$

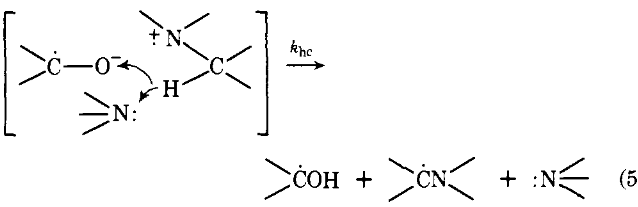
However, the effect is continuous after the change in concentration of ketone and the same curvature is seen in the experiments in *tert*-butyl alcohol (Figure 2) in which the same concentration of benzophenone is used throughout. Any possible effect of high amine concentration in *tert*-butyl alcohol in increasing the alkalinity of the medium and thus increasing disproportionation relative to combination of ketyl radicals and their ions[17] would lead to an observed decrease in quantum yield of reduction which is opposite to what is found.

The curvature describes a situation in which the increase in quantum yield with increase in amine concentration observed over a range of low concentrations is inadequate to predict the increase in quantum yield observed at still higher concentrations; and the decrease in quantum yield with decreasing concentration of amine at high concentrations predicts by extrapolation a greater decrease in quantum yield than is observed at low concentration. This behavior is consistent with reaction proceeding by two mechanisms. We suggest the normal one occurs at low concentration of amine ($<0.02\ M$) via eq 1 and described kinetically by eq 2 and, at higher concentration of amine, an additional reaction course higher than first order in amine. Our earlier studies were carried out largely over an apparently reasonable but limited range of concentrations in the medium and high concentration regions. They led to the high quantum yields characteristic of this domain. The limited range led to apparently linear plots of φ^{-1} vs. $(\text{amine})^{-1}$ and to essentially correct values of k_{ir}, but to high values for k_d. The value of k_d is derived from the dependence of quantum yield on concentration of reducing agent, and the high slope and low intercept of the plots of high concentration data led to this result.

The reactions might become more efficient at high amine concentrations if amine is present in the solvation shell or complexed with the ketone, and the excited ketone need not diffuse to amine, or could have a more favorable k_h/k_e ratio by reacting in the complexed state, or, conceivably, by reacting from the excited singlet state. Evidence for ground state complexation may be seen in the shift in $\lambda_{\max}$ for benzophenone to longer wavelengths and in a development of a wider envelope in the presence of high concentration of amine in both benzene and *tert*-butyl alcohol. Interaction of high concentration of amines with fluorenone apparently led to singlet quenching rather than to high singlet reactivity.[11-14] One might expect k_h/k_e to be less favorable in the spin allowed singlet quenching. Also the high rate and efficiency of intersystem crossing of benzophenone as compared with fluorenone make singlet reactivity an unlikely explanation. This was examined by study of quenching by piperylene of the photoreduction of benzophenone by 1 M cyclohexylamine in benzene and *tert*-butyl alcohol where the quantum yields are ~60% greater than would be expected from the low concentration values. The linear relationship of plots of φ^{-1} vs. (Q) (Figures 5 and 6) over the observed high extent of quenching (>85%) indicated normal behavior of the quencher. The excited ketone reacts with amine in solution and is subject to quenching. No unusual singlet reactivity not subject to triplet quencher is indicated.

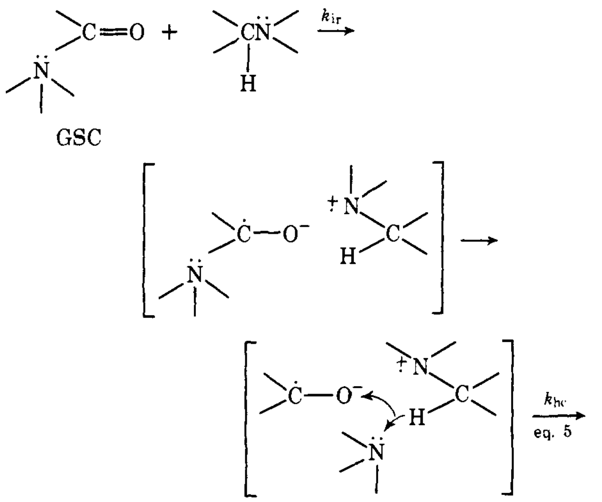
Comparison of quenching efficiency at high and low concentrations of amine was made by study of the effects of naphthalene on the 4-benzoylbenzoate–triethylamine system in aqueous pyridine at pH 12 (Table IV). The slopes of the plots of $1/\varphi$ vs. (Q) and the ratios of slopes to intercept $k_q/[k_d + k_{ir}(\text{RH})]$ are necessarily quite different at the two concentrations of amine, but the values of k_q/k_{ir} are essentially the same, 2.9 and 3.0. Since the quenchers are behaving normally, the values of k_{ir} are the same at the high and low concentrations. The reactions proceed over the whole range of concentration by initial charge-transfer interaction k_{ir}, with which quenchers interfere as usual by interaction with triplets. Values of k_{ir} are found to be similar at high and low amine concentrations, in the other systems also (Table V).

The reaction of higher order in amine may be formulated as an amine mediated transfer of the proton in the complex. A second molecule of amine abstracts H from the cation radical and transfers it to the anion radical (eq 5). A related involvement of amine in proton abstraction from α-C of an amine derived cation radical has been proposed in the anodic oxidation of *N,N*-dimethylbenzylamine.[18] In methanol-tetra-*n*-butylammonium fluoroborate, a second molecule of dimethylbenzylamine acts to abstract H from the electrolytically formed cation radical. Hydrogen is abstracted preferentially from the methyl groups, as has been observed in photoreduction by amines.[3] Anodic oxidation in 0.47 *M* potassium hydroxide in methanol, where hydroxide or alkoxide may abstract the proton, did not show such preference.[18]



(5)

Catalysis of hydrogen transfer by amine in the CTC may arise if ground state ketone is in equilibrium with a ketone-amine complex (GSC) which, after excitation, interacts with an amine molecule in solution, forming a CTC in which the initial complexing amine is present and catalyzes the hydrogen transfer (eq 6).



(6)

In the following equations, B is the ground state ketone, AH_2 the amine, and k_d has the value determined at low concentrations of amines or from direct measurement of triplet decay or quenching. Reactions in the absence of effects due to higher order of amine are as follows, and steady state approximations are applied.

$$B \xrightarrow{h\nu} {}^1B^* \xrightarrow{\text{isc}} {}^3B^* \quad \varphi_{\text{isc}} \sim 1 \qquad I_{\text{abs}} \tag{7}$$

$$^3B^* \xrightarrow{k_d} B \tag{8}$$

$$^3B^* + AH_2 \xrightarrow{k_{ir}} CTC \tag{9}$$

$$^3B^* + Q \xrightarrow{k_q} B + Q^* \tag{10}$$

$$CTC \xrightarrow{k_h} BH\cdot + AH\cdot \tag{11}$$

$$CTC \xrightarrow{k_e} B + AH_2 \tag{12}$$

$$AH\cdot + B \rightarrow A + BH\cdot \qquad \text{factor, } a \tag{13}$$

$$-d(B)/dt = ak_h(CTC) \tag{14}$$

$$d(CTC)/dt = 0 = k_{ir}(^3B^*)(AH_2) - k_h(CTC) - k_e(CTC) \tag{15}$$

$$(CTC) = k_{ir}(^3B^*)(AH_2)/(k_h + k_e) \tag{16}$$

$$d(^3B^*)/dt = 0 = I_{abs} - k_d(^3B^*) - k_{ir}(^3B^*)(AH_2) - k_q(^3B^*)(Q) \tag{17}$$

$$(^3B^*) = I_{abs}/[k_d + k_{ir}(AH_2) + k_q(Q)] \tag{18}$$

$$(CTC) = I_{abs}k_{ir}(AH_2)/(k_h + k_e)[k_d + k_{ir}(AH_2) + k_q(Q)] \tag{19}$$

$$-d(B)/dt/I_{abs} = \varphi = ak_hk_{ir}(AH_2)/(k_h + k_e)[k_d + k_{ir}(AH_2) + k_q(Q)] \tag{20}$$

$$\varphi^{-1} = \frac{(k_h + k_e)[k_d + k_{ir}(AH_2) + k_q(Q)]}{ak_hk_{ir}(AH_2)} \tag{21}$$

Since $f = k_h/(k_h + k_e)$, eq 21 is identical with eq 2 and constitutes derivation of eq 2.

At the low concentration ranges in the several systems, and over the entire range for 2-butylamine in 1:1 pyridine-water, the extrapolated limiting quantum yields (φ_{lim}, Table V) are the values af. It is likely that a is constant in these experiments and probably has the value 2 in the nonaqueous systems, the reaction of eq 4 being efficient. The fraction $f = k_h/(k_h + k_e)$ is affected by the structure of ketone and amine, by steric factors,[3,19] by the acidity of the cationic part and the basicity of the anionic part of the CTC,[19] and by the stability of the CTC which, if excessive, may favor k_e over k_h.[15] The value of f is also affected by the medium, which may assist in the transfer of the proton and favor k_h, or make the CTC excessively stable, favoring k_e.[16] In the benzophenone-cyclohexylamine system, values of f are 0.30 in benzene and 0.40 in *tert*-butyl alcohol, and k_h $\sim 0.43k_e$ in benzene and $0.67k_e$ in *tert*-butyl alcohol. The hydroxylic solvent, rendered basic by the amine, favors the transfer of the proton and increases k_h/k_e and quantum yield for photoreduction. In the aqueous systems, where the product is hydrol, $a = 1$, $f = 0.57$ for triethylamine, $k_h = 1.3k_e$, $f = 0.61$ for 2-butylamine, $k_h = 1.6k_e$. Hydrogen transfer in the CTC (k_h) is favored over quenching (k_e) by change from the organic to the alkaline aqueous solvent.

At low amine concentrations, eq 2 may be used for evaluation of both k_q/k_{ir} and k_d/k_{ir}, and k_{ir} and k_d values are found similar to those observed from phosphorescence quenching and decay. This treatment is inadequate at high amine concentrations. If a ground-state complex of ketone and amine ($B{:}AH_2$) absorbs part of the light and is excited, its geometry may be such that the complexed amine does not lead readily to the CTC. The amine may coordinate with the aromatic system. The excited complex $B^*{:}AH_2$ may react with amine in solution to form a CTC in which amine facilitated proton transfer (k_{hc} eq 6) or quenching may occur. The equations may be modified as follows.

$$B + AH_2 \rightleftarrows B{:}AH_2 \qquad K_{22} \tag{22}$$

$$B,\ B{:}AH_2 \xrightarrow{h\nu} {}^1B^*,\ {}^1B^*{:}AH_2 \xrightarrow{\text{isc}} {}^3B^*,\ {}^3B^*{:}AH_2 \tag{7c}$$

$$^3B^*,\ {}^3B^*{:}AH_2 \xrightarrow{k_d} B,\ B{:}AH_2 \tag{8c}$$

$$^3B^*,\ {}^3B^*{:}AH_2 + AH_2 \xrightarrow{k_{ir}} CTC,\ CTC{:}AH_2 \tag{9c}$$

$$^3B^*,\ {}^3B^*{:}AH_2 + Q \xrightarrow{k_q} B,\ B{:}AH_2 + Q^* \tag{10c}$$

$$\mathrm{CTC} \xrightarrow{k_h} \mathrm{BH}\cdot + \mathrm{AH}\cdot \qquad (11)$$

$$\mathrm{CTC} \xrightarrow{k_e} \mathrm{B} + \mathrm{AH_2} \qquad (12)$$

$$\mathrm{CTC{:}AH_2} \xrightarrow{k_{hc}} \mathrm{BH}\cdot + \mathrm{AH}\cdot + \mathrm{AH_2} \qquad (11c)$$

$$\mathrm{CTC{:}AH_2} \xrightarrow{k_{ec}} \mathrm{B{:}AH_2} + \mathrm{AH_2} \qquad (12c)$$

If we make the simplifying approximations that the initial complexation does not affect significantly the light absorbed and intersystem crossing, and that values of k_d and k_{ir} are the same for $^3\mathrm{B}^*{:}\mathrm{AH_2}$ as for $^3\mathrm{B}^*$, eq 7c-10c are equivalent to equations 7-10. The effects of complexation would depend on the fraction of ketone complexed and be due to more efficient hydrogen transfer in CTC:AH$_2$, to the more favorable ratio $f_c = k_{hc}/(k_{hc} + k_{ec})$ as compared with $f = k_h/(k_h + k_e)$. Equation 14 for disappearance of ketone is modified to eq 14c.

$$-\mathrm{dB}/\mathrm{d}t = a[k_h(\mathrm{CTC}) + k_{hc}(\mathrm{CTC{:}AH_2})] \qquad (14c)$$

Introduction of equations analogous to and in addition to eq 15-18 for d(CTC:AH$_2$)/dt, (CTC:AH$_2$), d(^{3}B*:AH$_2$)/dt, and (^{3}B*AH$_2$) leads to an expression for the quantum yield for reduction of ketone by interaction of both excited ketone and excited ketone-amine complex with amine (eq 20c and 2c) in which α is the fraction of ground state ketone which is complexed with amine.

$$\varphi = ak_{ir}(\mathrm{AH_2})[f(1-\alpha) + f_c(\alpha)]/[k_d + k_{ir}(\mathrm{AH_2}) + k_q(\mathrm{Q})] \qquad (20c)$$

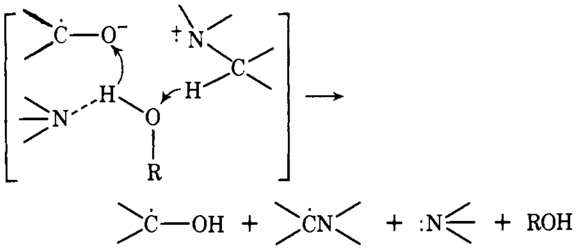
$$\varphi^{-1} = 1/a[f(1-\alpha) + f_c(\alpha)] + k_d/ak_{ir}(\mathrm{AH_2})[f(1-\alpha) + f_c(\alpha)] + k_q(\mathrm{Q})/ak_{ir}(\mathrm{AH_2})[f(1-\alpha) + f_c(\alpha)] \qquad (2c)$$

At constant amine concentration, high or low, a linear plot of φ^{-1} vs. (Q) would be obtained, allowing evaluation of k_{ir}. In the absence of quencher, a plot of φ^{-1} vs. $(\mathrm{AH_2})^{-1}$ would not be linear, as observed.

If ground-state complexing and its effects are observed at <ca. 0.05 M amine, the approximation may be made that, in the organic solvents, the extrapolated high concentration quantum yield arises from fully complexed ketone and is equal to af_c. In the benzophenone-cyclohexylamine system, values of f_c are 0.55 in benzene, compared with $f = 0.30$, and $f_c = 0.75$ in *tert*-butyl alcohol compared with $f = 0.40$, $k_{hc} = 1.2k_{ec}$ in benzene, $k_{hc} = 3.0k_{ec}$ in *tert*-butyl alcohol. If quenching in the CTC is unaffected by presence of amine, i.e., if $k_{ec} = k_e$, $k_{hc} = 2.8k_h$ in benzene, $k_{hc} = 4.5k_h$ in *tert*-butyl alcohol. From f_c, f, and values of quantum yields at intermediate concentrations of amine, Tables I and II, and application of eq 20c, values of α and K_{22}, the equilibrium constant for ketone-amine association, may be calculated. At 1 M cyclohexylamine in benzene, $\varphi = 1.04$, $\alpha = 0.88$, $K_{22} = 8\ M^{-1}$; at 0.2 M cyclohexylamine, $\varphi = 0.85$, $\alpha = 0.52$, $K_{22} = 6\ M^{-1}$; at 0.1 M cyclohexylamine, $\varphi = 0.77$, $\alpha = 0.40$, $K_{22} = 8\ M^{-1}$; and at 0.05 M cyclohexylamine, $\varphi = 0.71$, $\alpha = 0.26$, $K_{22} = 10\ M^{-1}$. Similar treatment of the data in Table II leads to $K_{22} = 3 \pm 1\ M^{-1}$ in *tert*-butyl alcohol over the range of 1-0.09 M cyclohexylamine. However, in this case, the amine may catalyze by making a solvent molecule more basic and more effective in abstracting a proton from the radical cation and transferring it to the radical anion.

The higher order effect of amine on quantum yield is much less in the alkaline aqueous pyridine. In reduction by triethylamine, the low concentration values should be used for evaluation of k_d/k_{ir} and k_d, but the difference between values at high and low concentration ranges is only a factor of 2 rather than more than an order of magnitude as seen in the organic solvents. In both ranges, the same value of k_{ir} is found. In reduction by 2-butylamine, no effect of concentration of amine is observed. The primary amine, more strongly hydrogen bonded and solvated by water, shows no effect over that provided by the solvent itself. The value of k_d/k_{ir} and the dependence of quantum yield on concentration of 2-butylamine are comparatively high because of the relatively low value of k_{ir} for interaction with the highly solvated primary amine. The limiting quantum yield is high because of the effect of the alkaline medium in facilitating proton transfer. In the hydrocarbon and alcohol solvents, proton transfer without catalysis by amine is inefficient while, at high amine concentration, the reduction may become as efficient as in the aqueous system, as catalysis of transfer by amine becomes similar to that by the aqueous medium.

We suggest that catalysis by amine in the nonaqueous media arises via amine which is initially complexed with ground-state ketone, and study of such complexes will be described later. The amine may act in a more general way, as a proton transfer agent in the medium which increases the k_h/k_e ratio in the normal charge transfer complex. The extrapolated quantum yield at high amine concentration in benzene, $\varphi = 1.1$, is that for photoreduction in a neat primary amine.[2] The value of f_c of 0.55, $k_{hc} = 1.2k_e$, may relate to the situation in which all the proton transfer is amine mediated (eq 5) in a medium of low dielectric constant; in the absence of amine catalysis (eq 1), $f = 0.30$, $k_h = 0.43 \cdot k_e$. In *tert*-butyl alcohol proton transfer is more efficient, $f_c = 0.75$, $k_{hc} = 3.0k_e$. This may be formulated as a modification of the amine mediated process of eq 5:



(23)

At still higher concentrations of amine in *tert*-butyl alcohol, quantum yields would decrease, approaching the value in neat amine. Small additions of alcohol to neat amine should increase quantum yields. Other studies in progress indicate that a variety of compounds in relatively low concentration may affect quantum yields, presumably by affecting the k_h/k_e ratio.

Acknowledgment. This work was supported by the National Science Foundation (GP 32452).

References and Notes

(1) (a) S. G. Cohen and J. I. Cohen, *J. Am. Chem. Soc.*, **89**, 164 (1967); (b) *J. Phys. Chem.*, **72**, 3782 (1968).
(2) S. G. Cohen and H. M. Chao, *J. Am. Chem. Soc.*, **90**, 165 (1968).
(3) S. G. Cohen and N. M. Stein, *J. Am. Chem. Soc.*, **93**, 6542 (1971).
(4) S. G. Cohen, G. A. Davis, and W. D. K. Clark, *J. Am. Chem. Soc.*, **94**, 869 (1972).
(5) For a general review on photoreduction by amines, see S. G. Cohen, A. Parola, and G. H. Parsons, Jr., *Chem. Rev.*, **73**, 141 (1973).
(6) W. H. Moore, G. S. Hammond, and R. B. Foss, *J. Am. Chem. Soc.*, **83**, 2789 (1961).
(7) W. D. K. Clark, A. D. Litt, and C. Steel, *J. Am. Chem. Soc.*, **91**, 5413 (1969).
(8) S. G. Cohen and A. D. Litt, *Tetrahedron Lett.*, 837 (1970).
(9) J. A. Bell and H. Linschitz, *J. Am. Chem. Soc.*, **85**, 528 (1963).
(10) S. G. Cohen and J. I. Cohen, *Isr. J. Chem.*, **8**, 757 (1968).
(11) (a) S. G. Cohen and J. B. Guttenplan, *Tetrahedron Lett.*, 5353 (1968); (b) J. B. Guttenplan and S. G. Cohen, *ibid.*, 2125 (1969).
(12) G. A. Davis, P. A. Carapellucci, K. Szoc, and J. D. Gresser, *J. Am.*

Chem. Soc., **91**, 2264 (1969).
(13) L. A. Singer, *Tetrahedron Lett.*, 923 (1969).
(14) R. A. Caldwell, *Tetrahedron Lett.*, 2121 (1969).
(15) G. H. Parsons, Jr., and S. G. Cohen, *J. Am. Chem. Soc.*, **96**, 2948 (1974).
(16) A. Parola, Ph.D. Thesis, Brandeis University, 1974.
(17) S. G. Cohen, G. C. Ramsay, N. M. Stein, and S. Y. Weinstein, *J. Am. Chem. Soc.*, **96**, 5124 (1974).
(18) J. E. Barry, M. Finkelstein, E. A. Mayeda, and S. D. Ross, *J. Org. Chem.*, **39**, 2695 (1974).
(19) G. H. Parsons, Jr., L. T. Mendelson, and S. G. Cohen, *J. Am. Chem. Soc.*, **96**, 6643 (1974).

Chemistry of Singlet Oxygen. XXI. Kinetics of Bilirubin Photooxygenation[1]

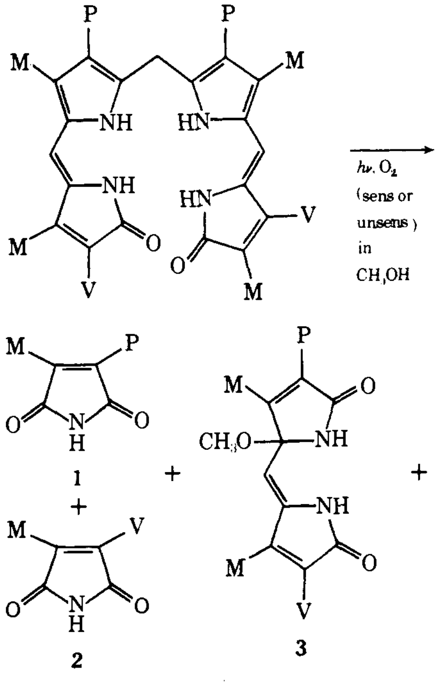
Christopher S. Foote*[1] and Ta-Yen Ching

Contribution No. 3440 from the Department of Chemistry, University of California, Los Angeles, California 90024. *Received February 6, 1975*

Abstract: The photooxidation of bilirubin in chloroform has been studied kinetically by several independent techniques. The rate of total consumption of singlet oxygen ($k_Q + k_R$) is $2.5 \times 10^9\ M^{-1}\ \mathrm{sec}^{-1}$. The value for reaction alone (k_R) is $0.4 \times 10^9\ M^{-1}\ \mathrm{sec}^{-1}$. The value for k_R is significantly higher than that determined by Matheson and Lee (in Freon 113); reasons for the discrepancy are discussed. The large value of k_R is consistent with the rapid disappearance of bilirubin during phototherapy of neonatal jaundice and may explain why side effects of this treatment are rare.

A common problem among newborn, especially premature, infants is jaundice; untreated, brain damage may result. The cause of the jaundice is insufficient activity of a hepatic system which effects the conversion of the lipid-soluble yellow pigment, bilirubin (BR), to its water-soluble glucuronic acid conjugate. The resulting excess BR deposits in the skin and brain of the infant. The common treatment for neonatal jaundice is irradiation of the infant with light in the wavelengths absorbed by BR (centered at 450 nm). Irradiation bleaches the BR in the skin, apparently by a photooxidative mechanism, and seems to prevent brain damage.[2-4]

The photooxidation of BR in vitro has been studied by several groups. The products (**1-4**) are those which might be expected from singlet oxygen attack.[5,6] The products apparently derive from cleavage of enamine double bonds and by 1,4 addition of oxygen to pyrrole rings. Both processes have ample precedent in singlet oxygen chemistry.



M = CH_3 V = $-CH{=}CH_2$ P = $-CH_2CH_2CO_2H$

Singlet oxygen, formed by BR as sensitizer, has been shown to be the reactive intermediate in the destruction in vitro.[7,8] Singlet oxygen sensitizers increase the rate of BR disappearance, and singlet oxygen quenchers inhibit it. The photooxidation rate increases five-fold in CD_3OD compared with CH_3OH,[7] which is evidence for the intermediacy of singlet oxygen, which has a longer lifetime in deuterated than in protiated solvents. BR can also photosensitize the oxidation of singlet oxygen acceptors but is a comparatively poor sensitizer compared with common sensitizing dyes.[7]

$$\begin{tikzcd}
\mathrm{BR} \arrow[r, "h\nu"'] & {}^1\mathrm{BR} \arrow[r, "\text{small fract}"'] & {}^3\mathrm{BR} \arrow[r, "O_2"'] & {}^1O_2 \arrow[r, "\mathrm{BR}"'] & \text{soluble products} \\
\mathrm{Sens} \arrow[r] & {}^1\mathrm{Sens} \arrow[r, "\text{large fract}"'] & {}^3\mathrm{Sens} \arrow[ur, "O_2"'] & &
\end{tikzcd}$$

Because systems which generate singlet oxygen have been shown to produce a variety of damage (called photodynamic) in numerous organisms,[9] one might anticipate some photodynamic damage to infants during phototherapy, although bilirubin is quite rapidly degraded. Only a few reports have appeared: Odell and coworkers reported photolytic hemolysis of blood samples to which bilirubin had been added and suggested that this hemolysis was responsible for an anemia which they believe is associated with phototherapy.[10] Odell had earlier reported photodynamic damage to serum albumin sensitized by bilirubin.[11]

Because of its medical importance and chemical interest, a careful mechanistic study of the photooxygenation of BR is overdue. BR might be expected to be highly reactive toward singlet oxygen as a result of its high electron density.

Recently, several types of singlet oxygen acceptors have been shown both to react with singlet oxygen and to quench it without reaction. Sulfides were the first class of substrate for which this behavior was identified;[12] more recently, certain phenols (in particular α-tocopherol)[13] and indenes[14] have been found to have similar behavior. We therefore thought it important to test for this behavior with BR as