

PHOTODIMERIZATION OF DIBENZ[*b,f*]AZEPINE DERIVATIVES AND THEIR REACTION INTERMEDIATES

KAZUO ASHIKAGA, SHINZABURO ITO, MASAHIDE YAMAMOTO[†] and YASUNORI NISHIJIMA

Department of Polymer Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606 (Japan)

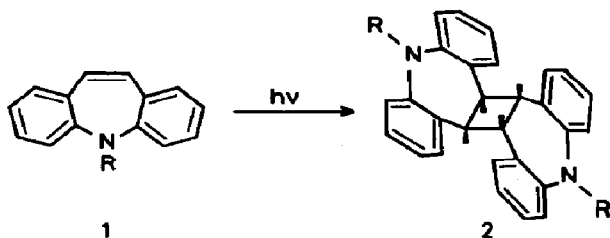
(Received October 21, 1986; in revised form January 6, 1987)

Summary

It is clearly demonstrated that the photodimerization of 5-acyl dibenz[*b,f*]azepine (DBA) derivatives occurs via excited triplet intermediates. The excited triplet state of 5-acyl DBA derivatives is barely formed on direct excitation, but is formed efficiently by triplet-triplet (T-T) energy transfer from a triplet sensitizer. Benzophenone-sensitized photoexcitation gave a unique reaction product, the *anti*-cyclobutane dimer of DBA. Under the sensitized conditions, the quantum yield for the photodimerization was estimated to be 0.15 at 25 °C ($[DBA] = 2.0 \times 10^{-3} \text{ mol l}^{-1}$). The triplet intermediate of this reaction was detected by nanosecond laser photolysis and the kinetic parameters of the triplet species were determined.

1. Introduction

5*H*-Dibenz[*b,f*]azepine (1a) (iminostilbene, DBA) and its derivatives are well-known chemicals in pharmacology [1], especially the compound having a γ -dialkylaminopropyl substituent at the 5-position, which is known to be physiologically active as an antidepressant [2].



- 1
- 2
- a: $R \equiv H$
 b: $R \equiv \text{COCH}_3$
 c: $R \equiv \text{COCH}_2\text{CH}_3$
 d: $R \equiv \text{CO}(\text{CH}_2)_2\text{CH}_3$
 e: $R \equiv \text{CO}(\text{CH}_2)_3\text{CH}_3$

[†] Author to whom correspondence should be addressed.

Many reports have appeared on the synthesis of 5-substituted derivatives of this compound in the patent literature. A detailed review with respect to DBA and related ring systems has been written by Kricka and Ledwith [3]. The photochemical reactivities of DBA derivatives have also been studied by Ledwith and coworkers [4]. They reported that triplet-sensitized and direct excitation of 5-acetyl DBA (1b) and other 5-acyl DBA derivatives result in the formation of their cyclobutane dimers. Herein, we report on the features of the photodimerization of 5-acyl DBA derivatives. Spectroscopic methods were applied to obtain information on the excited state of 5-acyl DBA derivatives; kinetic studies of the excited species were carried out by nanosecond laser photolysis to help clarify the behaviour of the excited triplet species.

2. Experimental details

2.1. Materials

1b was synthesized by the acetylation of 1a with acetic anhydride in the presence of a zinc chloride catalyst. A mixture of acetic anhydride and 1a in a molar ratio of 3:1 was heated with zinc chloride at 80 °C and stirred for 10 min. The reaction mixture was poured into ice-cooled water to form crystals. The crystallized product was filtered off, washed with water and dried. After recrystallization from ligroin several times, the product was purified by column chromatography on neutral alumina eluted with a mixture of dichloromethane and methanol (500:3). Finally, white needles of 1b were obtained.

Other compounds acylated at the 5-position of DBA, propionyl (1c), butyryl (1d) and valeryl DBA (1e), were prepared by the following procedure. First, the corresponding alkanoyl acid chloride was prepared from alkanecarboxylic acid by the reaction with thionyl chloride. Then, each acid chloride dissolved in dry benzene was added dropwise to a stirred solution of DBA in benzene at room temperature. The reaction mixture was refluxed for 5 h and then cooled and washed with water. The solution was dried with calcium chloride, and the evaporation of the solvent afforded a yellow oily product. The product was purified by a procedure similar to that for 1b.

Benzophenone was purified by recrystallization from ligroin several times and dried *in vacuo*.

Each solvent was purified in the usual way.

2.2. Spectroscopic measurements

Absorption spectra were measured by a Shimadzu UV-200S double-beam spectrophotometer. Fluorescence spectra were measured by a Shimadzu RF-502 spectrofluorometer, and phosphorescence spectra were taken using a Hitachi MPF-4 fluorescence spectrophotometer with a phosphorometry attachment.

An NEC SLG 2009 ruby laser was used for laser photolysis [5]. Details of the flash photolysis are given elsewhere [6]. Samples were excited by the second-harmonic pulse (347 nm, 16 ns, 3.02×10^{-8} einsteins pulse⁻¹). The phosphorescence lifetime of benzophenone at room temperature was measured by a single-photon counting method using an Ortec model 9200 system.

2.3. Photoirradiation

All sample solutions were photoirradiated in a thermostat at 25 °C. A Toshiba 300 W high pressure mercury lamp was used as the excitation light source. For unsensitized reactions, the 313 nm mercury line was selected through a combination of filters, which consisted of a Pyrex glass filter, a Toshiba UVD-25 filter and an aqueous solution filter of sodium carbonate (0.27 g l⁻¹) and potassium chromate (1 g l⁻¹) [7]. For sensitized reactions, the 365 nm mercury line was chosen by using a set of Toshiba UVD-2 and Corning C.S. 0-52 filters.

The sample solutions in a 1 cm quartz cell were deaerated by several freeze-pump-thaw cycles at about 10⁻⁶ Torr.

For the quantum yield measurements of the sensitized photodimerization, the concentrations of **1e** and benzophenone were adjusted to 2.0×10^{-3} mol l⁻¹ and 2.5×10^{-3} mol l⁻¹ respectively.

The number of photons at 365 nm was measured as 1.89×10^{-9} einsteins cm⁻² s⁻¹ by potassium ferrioxalate actinometry [8].

2.4. Product analysis

Photoproducts were analysed by a Toyo Soda HLC 802 UR gel permeation chromatography (GPC) instrument with double G2000HS columns (eluent, tetrahydrofuran).

IR spectra of photodimers were measured by a JASCO IR-G IR spectrophotometer and nuclear magnetic resonance (NMR) spectra (¹H, ¹³C) were obtained with a JOEL model FX-90Q spectrometer using tetramethylsilane as an internal standard. The spectroscopic data for the dimer **2b** are as follows. IR (KBr): 1660 cm⁻¹ (strong, C=O), 1445 cm⁻¹ (medium, methine C—H). ¹H NMR (CDCl₃): δ = 2.4 ppm (s, 6H, acetyl H), δ = 4.0 ppm (s, 4H, methine H), δ = 6.9 - 7.5 ppm (m, 16H, aromatic H). ¹³C NMR (CDCl₃): δ = 22.6 ppm (acetyl CH₃), δ = 48.4 ppm (methine CH), δ = 128.0 - 141.2 ppm (aromatic CH), δ = 173.2 ppm (acetyl C=O).

The precise structure of **2b** was determined by crystallographic analysis of X-ray diffraction data [9]. The dimer has an anti configuration. Other 5-acyl DBA derivatives also give only anti-type dimers.

3. Results and discussion

3.1. Photochemical reaction of **1b**

The reactivity of **1b** was examined in several kinds of solvent. The irradiation of the solutions with and without benzophenone was carried out

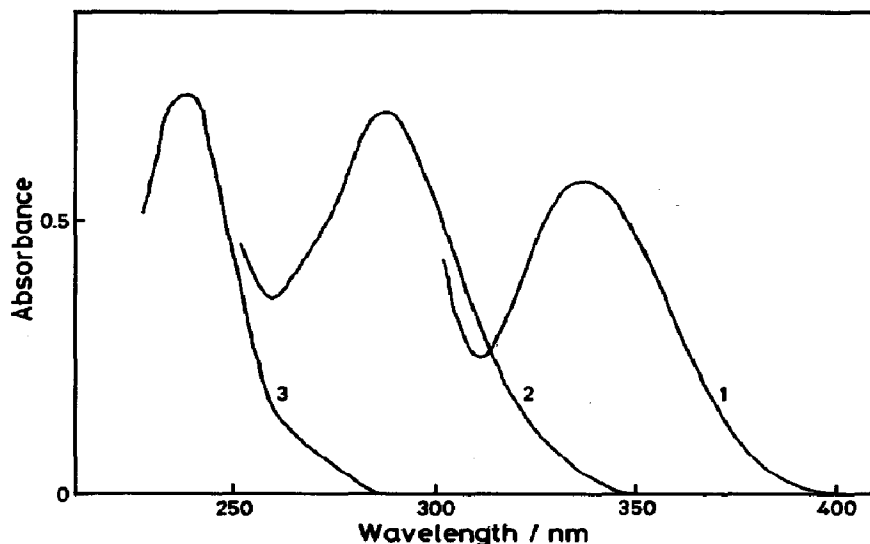


Fig. 1. Absorption spectra in dichloromethane: curve 1, benzophenone; curve 2, 1b; curve 3, 2b.

TABLE 1

Photodimerization of 1b in various solvents under sensitized and unsensitized conditions

Solvent	Dimer yield (%)	
	Sensitized irradiation ^a	Direct irradiation ^b
Benzene	72.3	0
Acetone	71.3	0
Methanol	59.4	0
Acetonitrile	83.3	0
Dichloromethane	72.6	0

The concentration of 1b was adjusted to be 6.5×10^{-2} mol l⁻¹ for all sample solutions. The concentration of benzophenone was adjusted to be 8.0×10^{-2} mol l⁻¹ for the sensitized samples. All sample solutions were irradiated for 2 h at room temperature.

^aExcited by 365 nm light.

^bExcited by 313 nm light.

at room temperature. Figure 1 shows the absorption spectra of 1b and its anti dimer 2b whose identification was described in Section 2.4. The absorption spectrum of a triplet sensitizer, benzophenone, is also given in Fig. 1. Benzophenone was selectively excited at the wavelength of 365 nm. In the course of irradiation of the sensitized samples, a crystalline product precipitated in benzene, acetone and methanol: the product came out of the reaction system because of its poor solubility. Furthermore, the dimer has a low absorbance at wavelengths longer than 300 nm in a good solvent such as dichloromethane. So, this dimer is not excited when the sample is excited at 365 nm. Table 1 shows the yields for 1b in various solvents.

The difference between the sensitized and direct excitation systems is clear, even though the numbers of absorbed photons were not corrected for the yields of the products in the photochemical reaction. Benzophenone-sensitized dimerization of 1b occurred in good yield, but dimerization in the unsensitized system was hardly observed. The same behaviour is also observed for other 5-acyl DBA derivatives. The product yields in the sensitized reaction of 1b depend on the kind of solvent employed. It is well known that the n, π^* state of aromatic ketones such as benzophenone causes hydrogen abstraction from hydrogen-donating compounds [10]. In methanol, the hydrogen abstraction reaction occurs competitively with T-T energy transfer to 1b and this suppresses the product yield. Table 1 also shows that the solvent polarity hardly affects the reaction yield of dimerization. In the experiments described below, dichloromethane was used as the solvent.

In contrast with the sensitized reaction, irradiation without benzophenone tinted the sample solution pale yellow and gave no dimeric product, contrary to the results reported by Ledwith *et al.* [4]. The absorption spectrum of the sample solution is similar to the spectrum of 1a, in that the absorption of the $n \rightarrow \pi^*$ transition of the nitrogen atom reappears. By reference to the photochemical reactions of *N*-acetyldiphenylamine and *N*-acetylcarbazole [11], this phenomenon suggests that 1b undergoes the photo-Fries rearrangement via its excited singlet state.

Next, the photochemical dimerization was examined kinetically. 1e was used since the solubility of this dimer in organic solvents is much better than that of 2b.

The relationship between the dimer yield and the photoirradiation time was examined by GPC. The irradiation time dependence of the dimer yield was examined between 10 and 30 min. The dimer yield increased linearly with increasing irradiation time. Next, the excitation light intensity dependence of the dimer yield was examined. In this experiment, the irradiation time was set to 30 min, and the intensity was varied in the range of 21.7% - 65.7% of the initial intensity by using several kinds of glass filter. The result showed that the yield of 2e is nearly proportional to the light intensity under these irradiation conditions.

In this sensitized photodimerization system, the quantum yield Φ_d of dimerization can be defined as follows:

$$\Phi_d = \frac{\text{number of product dimer molecules}}{\text{number of photons absorbed by the sensitizer}}$$

On the basis of this definition, the quantum yield of benzophenone-sensitized dimerization of 1e was estimated to be 0.15 under the conditions described in Section 2. Since the efficiency of triplet energy transfer from benzophenone to DBA is close to unity under these experimental conditions (more than 10^{-3} mol l⁻¹), Φ_d is nearly equal to the quantum yield defined by the ratio of the number of dimer molecules to the number of initial triplet DBA molecules produced through the sensitization.

3.2. Measurement of reaction intermediates

Fluorescence emission of **1b** was not detected on excitation at the various wavelengths in the various kinds of solvents. None of the other acylated DBA derivatives emitted fluorescence. Since 5-acyl DBA derivatives do not emit fluorescence, they would be expected to emit phosphorescence at a high efficiency at low temperatures. However, contrary to expectation, the observed phosphorescence is very weak (the phosphorescence quantum yield being below 10^{-4}). The triplet level E_T was determined to be 54 kcal mol⁻¹ from the phosphorescence spectrum. The other 5-substituted derivatives of DBA show identical phosphorescence spectra. The emission spectra undoubtedly originate from the excited triplet states, because the excitation spectra are consistent with the absorption spectra.

We tried to observe directly the excited triplet states for unsensitized and sensitized systems by nanosecond laser and flash photolysis. No transient absorption in the wavelength range 370 - 800 nm was observed on direct excitation for any of the 5-acyl DBA derivatives in dichloromethane. This fact shows that the efficiency of the intersystem crossing for 5-acyl DBA through the direct S_0 - S_1 excitation is very low. However, for the benzophenone-sensitized samples, the benzophenone triplet ($E_T = 69$ kcal mol⁻¹) is quenched by 5-acyl DBA and a new absorption band appears at the peak wavelength of 420 nm. Figure 2 shows the sensitized absorption spectrum of **1e** with the T-T absorption of benzophenone. The former was measured under the condition that the benzophenone triplet was completely quenched by **1e**. Since the quenching rate of benzophenone triplet agrees with the rise rate of the new absorption, this new absorption is identified as the T-T absorption of the 5-valeryl DBA derivative. The results show that triplet intermediates of 5-acyl DBA derivatives are not formed on direct

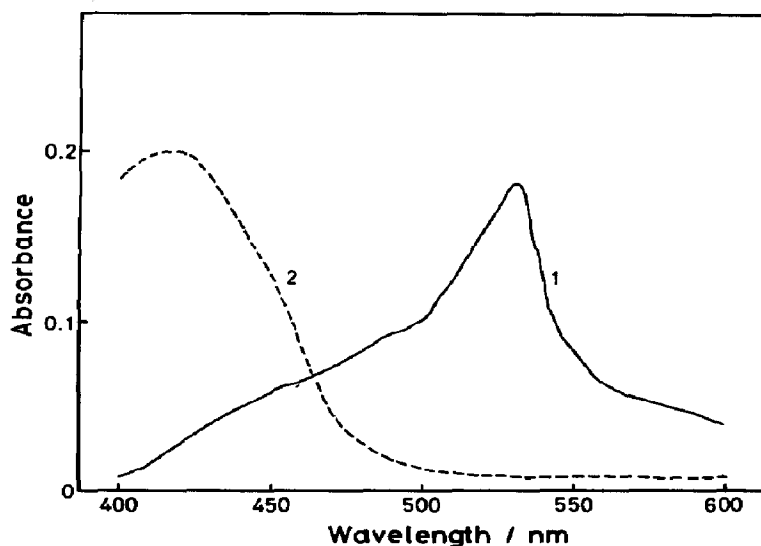


Fig. 2. T-T absorption spectra in dichloromethane at room temperature: curve 1, benzophenone; curve 2, **1e**. ($[BP] = 2.5 \times 10^{-3}$ mol l⁻¹; $[DBA] = 2.0 \times 10^{-3}$ mol l⁻¹.)

excitation, but are formed in good yield by T-T energy transfer from a triplet sensitizer such as benzophenone.

Next, creation and deactivation processes of the excited triplet states of benzophenone and DBA involving intermolecular T-T energy transfer are analysed according to the following kinetic scheme:



${}^1\text{D}$ and ${}^3\text{D}^*$ represent the ground state and the excited triplet state of the triplet energy donor, benzophenone, and ${}^1\text{A}$ and ${}^3\text{A}^*$ represent those of the energy acceptor, DBA. $\text{P}({}^1\text{A}-{}^1\text{A})$ represents the photoreaction product. In this system, the quantum yield of ${}^3\text{D}^*$ formation is assumed to be unity [7]. In the kinetic scheme, k_n^{D} and k_n^{A} are the sums of the rate constants of all unimolecular decay processes including radiative and non-radiative transitions for the triplet energy donor and the energy acceptor respectively. k_a^{D} and k_a^{A} are the bimolecular rate constants of T-T annihilation processes for the triplet energy donor and the acceptor respectively. k_t is the rate constant for T-T energy transfer from donor to acceptor, and k_r is that for the photochemical reaction of ${}^3\text{A}^*$ with ${}^1\text{A}$.

The rate constants in the scheme were determined by a laser photolysis technique. As shown in Fig. 2, there is almost no overlap between the T-T absorption of the 1e triplet and that of the benzophenone triplet, and thus the decay curves at 400 nm and 520 nm can be analysed unambiguously.

When benzophenone or sensitized 5-acyl DBA was excited at 347 nm by a low intensity laser pulse, the decay curves of T-T absorption were exponential. The lifetime of benzophenone was measured both by the single-photon-counting method and by low photon density laser photolysis in dichloromethane at room temperature. The lifetime τ_0^{D} of benzophenone obtained from laser photolysis under a low photon density (T-T absorption) agreed very closely with that obtained from the phosphorescence decay by the single-photon-counting method: $\tau_0^{\text{D}} = 3.6 \times 10^{-6}$ s in dichloromethane at room temperature. In contrast, excitation by a normal intensity pulse led to non-exponential decay curves. This phenomenon is probably due to a T-T annihilation process [12]. In the following laser photolysis, therefore, the laser power was attenuated by a suitable combination of filters so that the optical density of T-T absorption was no larger than 0.2. Under such conditions, the T-T annihilation rates become negligible.

The Stern–Volmer equation for the lifetime of the benzophenone triplet is expressed as follows:

$$\frac{\tau_0^D}{\tau^D} = 1 + \tau_0^D k_t [^1A] \quad (\text{I})$$

The plot of τ_0^D/τ^D against the concentration of 1e showed a straight line, and $k_t = 3.0 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ was obtained from the slope of this line. $k_n^D = 2.8 \times 10^5 \text{ s}^{-1}$ was obtained from the value of τ_0^D .

From the deactivation scheme, the following relationship between the triplet lifetime τ^A and the rate constants k_n^A and k_r for 1e was obtained:

$$\frac{1}{\tau^A} = k_n^A + k_r [^1A] \quad (\text{II})$$

The plot of $1/\tau^A$ against the concentration of 1e, $[^1A]$, showed a straight line. $k_n^A = 5.9 \times 10^4 \text{ s}^{-1}$ and $k_r = 2.4 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ were determined from the intercept and the slope of this straight line.

On the basis of the results described in this paper, the photochemical properties of 5-acyl DBA derivatives are summarized as follows.

(1) Photodimerization of 5-acyl DBA derivatives occurs efficiently via their excited triplet states, whose lifetime ($1/k_n^A$) is 17 μs at room temperature.

(2) Direct excitation of 5-acyl DBA derivatives gives no dimer product, but may lead to a photo-Fries rearrangement.

(3) Photodimerization of 5-acyl DBA derivatives is easily sensitized by a triplet sensitizer whose triplet energy level is higher than 54 kcal mol⁻¹.

(4) The quantum yield of dimerization is estimated to be 0.15 at $[\text{DBA}] = 2.0 \times 10^{-3} \text{ mol l}^{-1}$.

(5) The reaction yield of dimerization does not depend on the solvent polarity.

(6) The product of the sensitized photodimerization is found to be an anti-type dimer alone.

Acknowledgments

This work was supported by Grant-in-Aid for Scientific Research No. 61123006 from the Ministry of Education, Science and Culture of Japan.

References

- 1 F. Haflinger and V. Burckhardt, *Psychopharmacological Agents*, Vol. 1, Academic Press, New York, 1964, p. 35.
- 2 E. Jucker, *Angew. Chem., Int. Ed. Engl.*, 2 (1963) 493.
- 3 L. J. Kricka and A. Ledwith, *Chem. Rev.*, 74 (1974) 101.
- 4 L. J. Kricka, M. C. Lambert and A. Ledwith, *J. Chem. Soc., Chem. Commun.*, (1973) 244.

- L. J. Kricka, M. C. Lambert and A. Ledwith, *J. Chem. Soc., Perkin Trans. I*, (1974) 52.
- A. K. Alimoglu, C. H. Bamford, A. Ledwith and S. U. Mullik, *Macromolecules*, **10** (1977) 1081.
- C. H. Bamford, A. Ledwith and Y. Yagic, *Polymer*, **19** (1978) 354.
- 5 A. Tsuchida, M. Yamamoto and Y. Nishijima, *J. Phys. Chem.*, **88** (1984) 5062.
- 6 M. Yamamoto, M. Ohoka, K. Kitagawa, S. Nishimoto and Y. Nishijima, *Chem. Lett.*, (1973) 745.
- 7 S. L. Murov, *Handbook of Photochemistry*, Dekker, New York, 1973.
- 8 C. G. Hatchard and C. A. Parker, *Proc. R. Soc. London, Ser. A*, **235** (1956) 518.
- 9 J. P. Reboul, B. Cristau and J. C. Soyfer, *Acta Crystallogr., Sect. B*, **36** (1980) 2683.
M. M. Harding, *Acta Crystallogr., Sect. C*, **39** (1983) 397.
T. Taga, N. Yamamoto, K. Ashikaga and Y. Nishijima, *Acta Crystallogr., Sect. C*, **42** (1986) 840.
- 10 C. Walling and M. J. Gibian, *J. Am. Chem. Soc.*, **87** (1965) 3361.
S. G. Cohen and R. J. Bumgarten, *J. Am. Chem. Soc.*, **89** (1967) 3471.
A. Padwa, *Tetrahedron Lett.*, (1964) 3465.
A. V. Beuttner and J. Deninas, *J. Phys. Chem.*, **75** (1971) 187.
- 11 H. Shizuka, M. Kato, T. Ochiai, K. Matsui and T. Morita, *Bull. Chem. Soc. Jpn.*, **43** (1970) 67.
- 12 T. Takemura, H. Baba and M. Fujita, *Bull. Chem. Soc. Jpn.*, **46** (1973) 2625.