ELSEVIER

Journal of Photochemistry and Photobiology
B: Biology 28 (1995) 229–234

Journal of
PHOTOCHEMISTRY
AND
PHOTOBIOLOGY
B:BIOLOGY

Photochemistry of dibenzoyl methane UVA filters
Part 1

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Received 21 October 1994; accepted 11 January 1995

Abstract

Two dibenzoyl methane derivatives, 4-isopropyldibenzoyl methane (I-DBM) and 4-*t*-butyl-4′-methoxydibenzoyl methane (BM-DBM), have been found to be photolabile towards UVA light in non-polar solvents, whereas in polar solvents photodegradation was very low. In each case about a dozen photoproducts were identified: their formation involves primary α bond cleavages of carbonyl groups, followed by hydrogen abstraction and/or oxidation or radical recombination. These photoproducts can be classified as substituted benzaldehydes, benzoic acids, acetophenones, phenylglyoxals, benzils, dibenzoyl methanes or dibenzoyl ethanes.

Keywords: Sunscreen; Photodegradation; Photoproducts

1. Introduction

Protection against UVA sunlight by sunscreens has assumed increasing importance since more has become known about its harmful effects on human skin such as cutaneous photoaging and photocarcinogenesis.

Besides substituted benzophenones, dibenzoyl methane derivatives are widely used in UVA-absorbing sunscreens as well as in photoprotective cosmetics [1].

At present the most common among the dibenzoyl methanes is 4-*t*-butyl-4′-methoxydibenzoyl methane (BM-DBM), followed by 4-isopropyldibenzoyl methane (I-DBM). While BM-DBM has been approved for general use in Europe, I-DBM was struck off the European Union (EU) positive list effective from 30 June 1994.

High screening efficiency can only be guaranteed if a UV filter is of high photostability. The possible formation of photoproducts, their chemical reactions and their accumulation on/in human skin may have deleterious effects.

Therefore special attention should be paid to the photochemistry of screening agents. In a recent study, photodecomposition has been demonstrated for a solution of BM-DBM in cyclohexane by Roscher et al. [2]. However, their irradiation conditions were rather drastic ($\lambda > 185$ nm, 100 h). Deflandre and Lang [3] simulated a UVA sunscreen by incorporating dibenzoyl methanes in thin film layers of a model emulsion and found high degradation rates.

In the present paper it has been the authors' purpose to investigate the photochemistry of dibenzoyl methanes under solar simulation in various solvents. The results obtained should contribute to a stepwise approach from laboratory to natural conditions.

In the case of the two dibenzoyl methanes, photodegradation leads to numerous photoproducts (Table 1). The photochemical basis and the influencing parameters for the formation of these photoproducts are the subject of this article.

2. Materials and methods

2.1. Chemicals

I-DBM (Eusolex 8020) and BM-DBM (Eusolex 9020) were kindly and generously supplied by Merck (Darmstadt, Germany).

Benzaldehyde, cuminaldehyde, anisaldehyde, benzoic acid, *p*-anisic acid, *p-tert*-butyl acid and 4-methoxyacetophenone were obtained from Fluka (Neu-Ulm, Germany).

Acetophenone, benzil and phenylglyoxal monohydrate were purchased from Riedel-de-Haen (Seelze, Germany).

SSDI 1011-1344(95)07118-0

Table 1
Photoproducts of 4-isopropyldibenzoyl methane (I-DBM) and 4-*t*-butyl-4′-methoxydibenzoyl methane (BM-DBM) in cyclohexane. All compounds were identified by GC–MS analysis. Photoproducts marked with a 'prime' are almost detectable in unconcentrated samples (7 mmol, 8 h irradiation time)

	I-DBM	BM-DBM
Benzaldehydes	Benzaldehyde (**1a′**)	4-*t*-Butyl benzaldehyde (**1c**)
	4-Isopropyl benzaldehyde (**1b′**)	4-Methoxy benzaldehyde (**1d**)
Benzoic acids	Benzoic acid (**2a**)	4-*t*-Butyl benzoic acid (**2c**)
	4-Isopropyl benzoic acid (**2b**)	4-Methoxy benzoic acid (**2d**)
Phenylglyoxals	Phenylglyoxal (**3a′**)	4-*t*-Butyl phenylglyoxal (**3c′**)
	4-Isopropyl phenylglyoxal (**3b′**)	4-Methoxy phenylglyoxal (**3d**)
Acetophenones	Acetophenone (**4a**)	4-*t*-Butyl acetophenone (**4c′**)
	4-Isopropyl acetophenone (**4b′**)	4-Methoxy acetophenone (**4d**)
Benzils	Benzil (**5a′**)	4-*t*-Butyl-4′-methoxy benzil (**5c′**)
	4-Isopropyl benzil (**5b′**)	4,4′-Di-*t*-butyl benzil (**5d′**)
Dibenzoyl methanes		4,4′-Dimethoxydibenzoyl methane (**6c**)
Dibenzoyl ethanes	4-Isopropyldibenzoyl ethane (**7a′**)	4-*t*-Butyl-4′-methoxydibenzoyl ethane (**7c**)

4-Methoxyphenylglyoxal was synthesized by the following procedure. To 2.25 g of 4-methoxyacetophenone (15 mmol) a solution of 1.67 g of selenium dioxide (15 mmol; Fluka) in 34 ml of dioxan–water (16:1) was slowly added and the temperature kept below 20 °C during this time. The reaction mixture was stirred and heated under reflux for 6 h. The hot solution was filtered to separate precipitated selenium. A dilution with dioxan (1:100) was directly analysed by gas chromatography–mass spectrometry (GC–MS) to prove the identity of photoproduct **3d**.

The solvents used were of analytical grade (Merck). Cyclohexane-d_{12} and isopropanol-d_8 were purchased from Aldrich (Steinheim,Germany).

2.2. *Photolysis*

The photodegradation of I-DBM and BM-DBM was kinetically investigated in 3.5 mmol solutions of non-deaerated cyclohexane, isooctane, isopropanol and methanol. As irradiation source a solar simulator (SOL 500, Dr. K. Hönle G.m.b.H., Martinsried, Germany) was employed in combination with WG295 ($\lambda > 260$ nm) and WG345 ($\lambda > 320$ nm) glass filters (Schott Glaswerke, Mainz, Germany) at an irradiation surface of 16 cm^2. Irradiance measurements, recorded on a Dr. Hönle UV meter, showed 12.4 mW cm^{-2} UVA and 0.54 mW cm^{-2} UVB for the WG295 filter and 11.1 mW cm^{-2} UVA and 0 mW cm^{-2} UVB for the WG345 filter. Two quartz beakers (capacity 50 ml, diameter 38 mm), each containing a solution of the respective dibenzoyl methane, were simultaneously irradiated for up to 8 h. The solutions were stirred and water cooled (15 °C) in a quartz tube placed in front of the filters.

The progress of photodegradation was monitored by high performance liquid chromatography (HPLC) and GC–MS.

For HPLC a Jasco high pressure gradient system (Jasco Deutschland G.m.b.H., Gross Zimmern, Germany) was applied consisting of an autosampler (Jasco 851 AS), a variable UV detector (Jasco, UV 975), two HPLC pumps (Jasco PU-980) and a Bischoff (Leonberg, Germany) HPLC column (Nucleosil 120, C 8, 5 μm, 4.6 mm × 25 cm). Gradient: methanol/phosphate buffer (0.01 mol, pH 4), 20/80 (0 min) → 70/30 (30–45 min) → 95/05 (55 min). Flow rate: 0.8 ml min^{-1}. t_R (min): **2a** (detection at 233 nm) 13:06, **2b** (242 nm) 27:40 and I-DBM (254 nm) 49:30; **2c** (259 nm) 16:50, **2d** (242 nm) 28:70 and BM-DBM (260 nm) 51:00.

GC–MS analyses were performed on a Perkin–Elmer 8420: quartz capillary column (25 m, inner diameter 0.25 mm, PVMS 54 (phenylmethyl vinyl methyl silicon), 0.3 μm, He, 80 kPa, 27 cm s^{-1}); injection port 270 °C; temperature programme 100 °C → 200 °C/5 °C min^{-1}–200 °C → 270 °C/15 °C min^{-1}–20 min isothermal 270 °C; coupled with a Finnigan MAT (Bremen, Germany) Ion Trap 800, electron impact (EI) and positive methanol chemical ionization (CI) mode. t_R (min): **1a′** 4:09, **1b′** 8:43, **1c** 10:27, **1d** 9:01, **2a** 6:54, **2b** 12:57, **2c** 14:34, **2d** 12:49, **3a′** 5:32, **3b′** 11:17, **3c′** 12:54, **3d** 11:42, **4a** 5:27, **4b′** 11:05, **4c′** 12:45, **4d** 11:18, **5a′** 22:06, **5b′** 26:02, **5c′** 31:37, **5d′** 32:27, **6c** 36:03, I-DBM 29:29, BM-DBM 38:06, **7a′** 27:43, **7c** 34:51.

2.3 *Product isolation*

Isolation of photoproducts **2a** and **2b** was performed on a Bischoff (Leonberg, Germany) HPLC system (UV detector Lambda 1000, HPLC pump model 2200) using a semipreparative HPLC column (Bischoff, SNC + SPC, LiChrosorb RP18, 5 μm, 8 mm × 25 cm); flow rate 2 ml min^{-1}; detection at 237 nm; eluent methanol/water (50/50, changed to 80/20 after 13 min). After irradiation (45 h, WG295) of I-DBM in cyclohexane (80 mg/40 ml) the reaction mixture was evaporated to dryness, dissolved in methanol (1 ml) and subjected to HPLC (five injections, 200 μl each). Photoproduct **2a** was eluted after 12 min and photoproduct **2b** after 22 min.

2.4 *Spectra*

IR spectra (KBr discs) were measured on a Pye Unicam SP 1100 instrument (Cambridge, UK) and UV spectra with a Perkin-Elmer Lambda 2 (Überlingen, Germany). ^{13}C and ^1H nuclear magnetic resonance (NMR) spectra were recorded on a Bruker (Karlsruhe, Germany) AC-250 spectrometer (Me_4Si as internal standard; 63 and 250 MHz nominal frequency respectively).

2.5. *Data*

GC–MS. EI (70 eV) and positive methanol CI data of *m/z* values for fragments and their relative intensities (%) are given. Benzoyl cation fragments are indicated by bold digits.

1c (t_R=10:22), EI: 162 ($M^{\cdot+}$, 12), 147 (100), 119 (45), 103 (10), 91 (94), 77 (17), 65 (11), 57 (7); CI: 163 (MH^+, 100), 162 (4), **161** (2), 147 (1), 91 (6).

3b′ (t_R=11:17), EI: **147** (100), 119 (7), 104 (14), 103 (15), 91 (66), 78 (18), 77 (22); CI: 177 (MH^+, 100), **147** (7), 135 (7), 91 (7).

3c′ (t_R=12:54), EI: **161** (100), 146 (29), 133 (3), 131 (6), 118 (32), **105** (17), 91 (33), 76 (8), 57 (15); CI: 191 (MH^+, 100), 190 (5), **161** (3), 135 (2).

4b′ (t_R=11:05), EI: 162 ($M^{\cdot+}$, 9), **147** (100), 119 (10), 103 (12), 91 (38), 78 (13), 77 (17); CI: 163 (MH^+, 100), **147** (4).

4c′ (t_R=12:45), EI: 177 (7), 176 ($M^{\cdot+}$, 3), **161** (100), 146 (6), 133 (19), 118 (9), 105 (26), 91 (22), 77 (12); CI: 177 (MH^+, 100).

5b′ (t_R=26:02), EI: 252 ($M^{\cdot+}$, 1), **147** (100), 119 (6), **105** (28), 91 (30), 77 (40); CI: 253 (MH^+, 13), **147** (22), **105** (100).

5c′ (t_R=31:37), EI: 296 ($M^{\cdot+}$, 2), **161** (26), 146 (6), **135** (100), 118 (9), 107 (6), 92 (13), 91 (6), 77 (16); CI: 297 (MH^+, 13), **161** (100), **135** (13).

5d′ (t_R=32:27), EI: **161** (100), 146 (8), 118 (17), 105 (6), 91 (11), 77 (4); CI: 323 (MH^+, 17), **161** (100).

6c (t_R=36:03), EI: 284 ($M^{\cdot+}$, 59), 177 (7), **135** (100), 108 (65), 92 (26), 77 (37); CI: 285 (MH^+, 14), **135** (100).

7a′ (t_R=27:43), EI: 280 ($M^{\cdot+}$, 4), **147** (100), 119 (5), **105** (31), 91 (26), 77 (39); CI: 281 (MH^+, 100), **147** (47), **105** (64).

7c (t_R=34:51), EI: 324 ($M^{\cdot+}$, 6), **161** (32), 146 (5), **135** (100), 118 (7), 92 (11), 77 (17); CI: 325 (MH^+, 100), **161** (44), **135** (20).

In the case of photoproducts **1a**′, **1b**′, **1d**, **2a**, **2c**, **2d**, **3a**′, **4a**, **4d** and **5a**′ the assignments were confirmed by comparing the MS data with those of the respective commercial samples available. The structure of **3d** was proved unequivocally by independent synthesis and comparison of the MS data. Photoproduct **2b** was isolated and characterized by UV, IR, ^{13}C and ^1H NMR and GC–MS.

2b. UV (MeOH): λ_{max} (nm) (logε) 236 (4.14). IR (cm^{-1}): 3360–2400, 2980, 1695, 1620, 1580, 1330, 1300, 1195, 860, 780.

^1H NMR (CD_3OD): δ 7.94 (d, 2H, ^3J=8.38 Hz), 7.33 (d, 2H, ^3J=8.29 Hz), 2.97 (sept., 1H, ^3J=6.92 Hz), 1.26 (d, 6H, ^3J=6.95 Hz).

^{13}C NMR (CD_3OD): δ 171.4, 157.0, 132.3, 130.9, 128.9, 36.8, 25.4.

GC–MS (t_R=12:57), EI: 164 ($M^{\cdot+}$, 24), 163 (7), 149 (100), 131 (39), 119 (59), 105 (88), 103 (56), 91 (35), 77 (69); CI: 165 (MH^+, 100), **147** (15), 123 (9), 105 (5).

3. Results

I-DBM and BM-DBM are both photodegraded in the non-polar solvents cyclohexane and isooctane but show photostability in the polar solvents isopropanol and methanol.

The decomposition rates were found to grow exponentially with increasing time of irradiation (Fig. 1). The percentage of I-DBM or BM-DBM disappearance depends on the filter employed. Using the WG345 filter, the photodegradation is about 8% for both DBMs. With the WG295 filter it is considerably higher: 20% for I-DBM and 14% for BM-DBM.

In correlation with the filter transmittance spectra (Fig. 2) it is assumed that photodegradation is not related to the long wave UV absorption of dibenzoyl methanes. In the case of a long wave $\pi\rightarrow\pi^*$ excitation as photochemical basis, higher degradation rates in the WG345 experiments would be expected. The $\pi\rightarrow\pi^*$ absorption bands in cyclohexane can be found in the ranges 290–390 nm (I-DBM) and 300–400 nm (BM-DBM). Their maxima are determined at 341 nm (logε=4.41) for I-DBM and 351 nm (logε=4.49) for BM-DBM.

On the contrary, it seems more likely that the photochemical behaviour could proceed through the excitation of dibenzoyl methanes in their 1,3-diketo forms. The excitation maxima are suggested to be comparable with those of related chromophores such as acetophenone, which displays an $n\rightarrow\pi^*$ absorption maximum in heptane at 320 nm (logε=1.6) [4].

Photoreaction through an $n\rightarrow\pi^*$ excited triplet state is also indicated by the structure of the identified photoproducts (Fig. 3). They all originate from two radical precursors, either from a benzoyl radical (**I**) or from a phenacyl radical (**II**). Seven groups of photoproducts are classified and listed in Table 1.

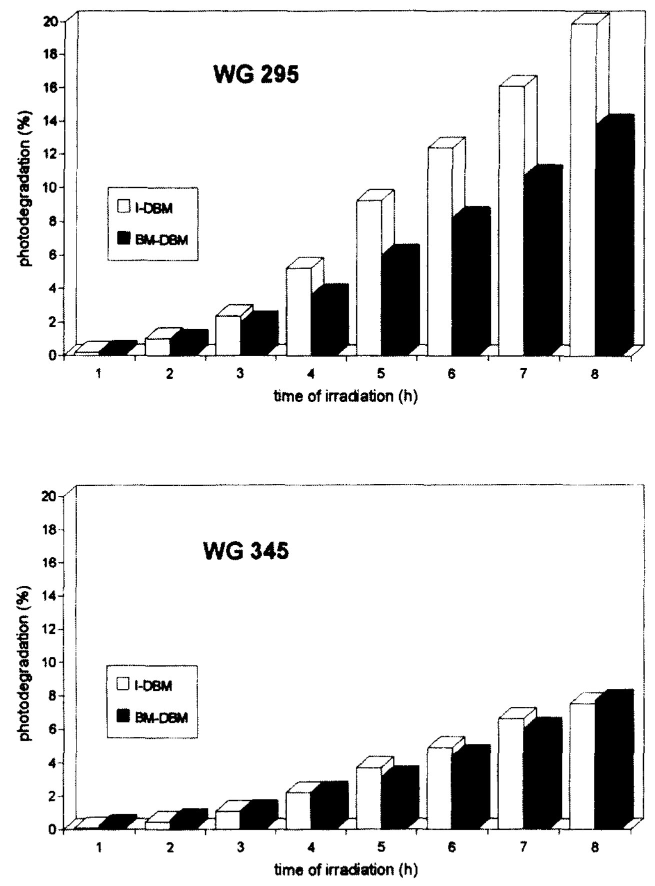

Fig. 1. Photodegradation of 4-isopropyldibenzoyl methane (I-DBM) and 4-*t*-butyl-4′-methoxydibenzoyl methane (BM-DBM) in cyclohexane. WG295, λ > 260 nm; WG345, λ > 320 nm.

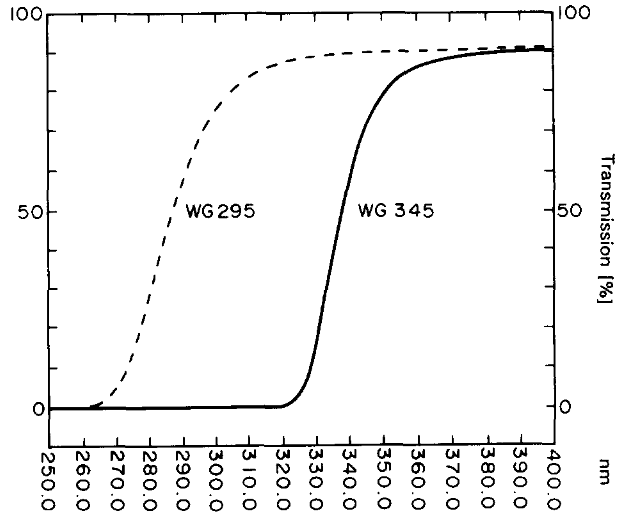

Fig. 2. Transmission spectra of filters employed for irradiation. WG295, λ > 260 nm; WG345, λ > 320 nm. $\pi \rightarrow \pi^*$ absorption bands of dibenzoyl methanes in cyclohexane: 290–390 nm (I-DBM); 300–400 nm (BM-DBM).

The reaction kinetics were monitored by means of HPLC quantitation of the main photoproducts. These are the benzoic acids **2a** and **2b** for I-DBM and **2c** and **2d** for BM-DBM.

The molar recovery of each photodegraded dibenzoyl methane, calculated in total acid, is about 50%. Reactive compounds, as shown in Fig. 3, and their possible reactions with the respective dibenzoyl methane might explain the remaining 50% photodegradation.

The benzoic acids are formed in reproducible ratios (**2a**/**2b** = 0.86 and **2c**/**2d** = 1.50). Their formation rates increase with increasing time of irradiation and are possibly affected by the presence of oxygen at the beginning of irradiation and its disappearance by acting as a triplet quencher. In fact, higher photostability is observed when irradiation is carried out under a continuous oxygen supply (Fig. 4). For I-DBM the degradation rate then is about one-third of that in the corresponding experiment without oxygen supply.

Sensitizing effects of acetophenones or other photoproducts could also play a role in the course of photodegradation (acetophenone, $E_T = 74$ kcal mol^{-1}; BM-DBM, $E_T = 59.5$ kcal mol^{-1} [5]).

Reactive photoproducts such as phenylglyoxals, aldehydes and benzils were identified by GC–MS analysis of the respective solutions in cyclohexane. The irradiated samples (WG295, 8 h, 7 mmol) were either directly subjected to GC–MS or first 5–10-fold concentrated under mild conditions (100 mbar, 40 °C). Some photoproducts (see Table 1) are almost detectable in the unconcentrated samples. GC–MS data are listed in Section 2.5.

Finally, it was of major interest to find out why photodegradation is observed in cyclohexane and isooctane whereas isopropanolic and methanolic solutions show remarkable stability.

Considering keto–enol tautomerism in both solvents, a possible answer can be given by ^{1}H NMR spectroscopic data. For each dibenzoyl methane, ^{1}H NMR measurements were carried out in cyclohexane-d_{12} and isopropanol-d_8 directly after dissolution and under the same conditions for each measurement (0.03 mol, 64 scans, room temperature). The following keto–enol tautomerisms are determined in cyclohexane-d_{12} by quantitative evaluation of the olefinic resonances of the respective enol-oxo forms.

I-DBM shows 1.7% diketo form. The olefinic proton of the enol-oxo form has a chemical shift $\delta = 6.73$ (s, 1H); the methylene resonance of the diketo form can be detected at $\delta = 4.40$ (s, 2H).

BM-DBM shows 3.5% diketo form. The respective resonances are $\delta = 6.66$ (s, 1H) and $\delta = 4.35$ (s, 2H). In every case the positions of the tautomerism equilibria are well on the side of the enol-oxo forms (I-DBM, 98.3%; BM-DBM, 96.5%).

In isopropanol-d_8, however, no methylene resonances of the 1,3-diketo forms are detectable and the integrals of the olefinic resonances are exactly the value of one proton. The chemical shifts of the olefinic protons in

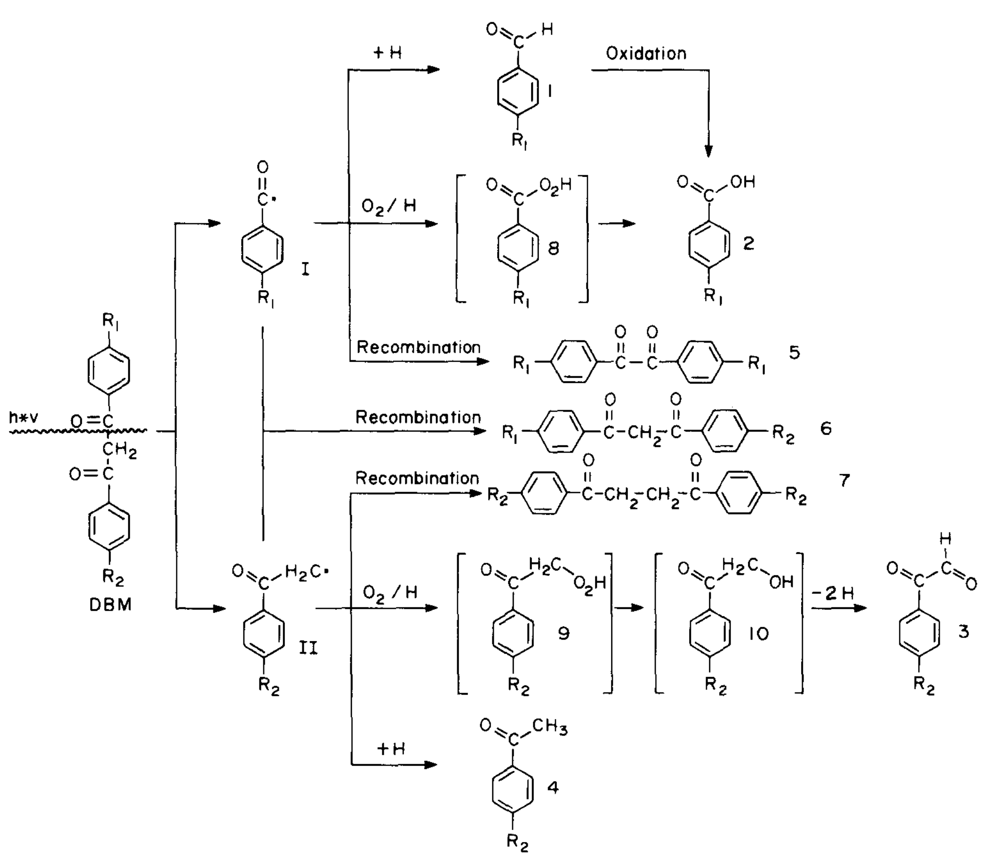

Fig. 3. Photodegradation scheme of dibenzoyl methanes (DBM) in model solutions. 4-Isopropyldibenzoyl methane (I-DBM): $R_1 \equiv H$, $R_2 \equiv -CH(CH_3)_2$. 4-*t*-Butyl-4′-methoxydibenzoyl methane (BM-DBM): $R_1 \equiv -OCH_3$, $R_2 \equiv -C(CH_3)_3$. R_1 and R_2 are mutually exchangeable for the respective dibenzoyl methane. **1**, Benzaldehydes; **2**, benzoic acids; **3**, phenylglyoxals; **4**, acetophenones; **5**, benzils; **6**, dibenzoyl methanes; **7**, dibenzoyl ethanes; **8**, perbenzoic acids; **9**, α-hydroperoxyacetophenones; **10**, α-hydroxyacetophenones. **I**, Benzoyl radicals; **II**, phenacyl radicals. Structures in brackets are proposed intermediates.

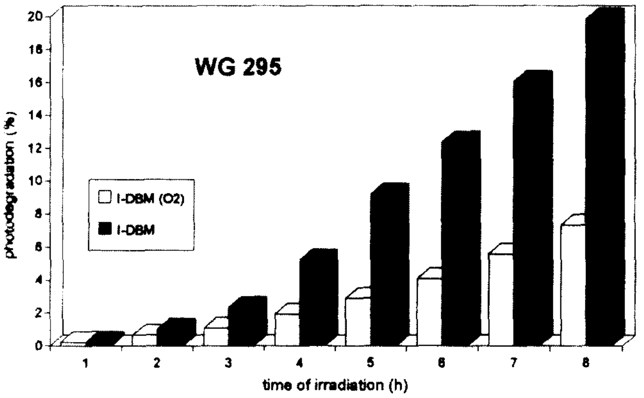

Fig. 4. Photodegradation of 4-isopropyldibenzoyl methane under continuous oxygen supply (I-DBM (O_2)) and without (I-DBM). WG295, λ>260 nm.

isopropanol are δ=6.97 (s, 1H) (I-DBM) and δ=6.90 (s, 1H) (BM-DBM).

In agreement with the photochemistry described above, it clearly appears that the photodegradation of I-DBM and BM-DBM depends strongly on the presence of the 1,3-diketo forms. Furthermore, the typical hydrogen abstraction by ketones in H donor solvents such as isopropanol is not observed at all.

4. Discussion

About a dozen photoproducts for each dibenzoyl methane were identified and in part quantified. A complete reaction path for all products is suggested in terms of solar simulation. In contrast, Roscher et al. [2] employed a high irradiance (λ>185 nm!) and a long irradiation time (100 h!) in their BM-DBM experiment. Under these conditions it is likely that the only photoproducts detectable were the relatively photostable benzoic acids **2c** and **2d**. We assume that all other primary photoproducts (Table 1) were converted into the respective benzoic acids owing to their experimental conditions.

For transference of the in vitro results to the in vivo application of a sunscreen product it is required to compare the experimental conditions under solar simulation with those under natural sunlight.

The radiation intensity of the solar simulator was about 2.5 times higher in UVA and 3.5 times higher in UVB than sunlight (June, mediterranean area [3]). However, it should be mentioned that photodegradation rates were determined in dilute solutions, so that an irradiation surface comparable with human skin was not simulated. Considering the effective surface as the main parameter for photodegradation, the dibenzoyl methanes might be photodegraded in even higher amounts when incorporated in thin film layers of a sunscreen preparation and exposed to sunlight on human skin.

This is in agreement with the work of Deflandre et al. who examined the photostability of I-DBM and BM-DBM in very thin film layers of an emulsion [3]. They found degradation rates up to 50% after an irradiation time of 1 hour only, but photochemical reactions have not been investigated.

Dibenzoyl methanes have the property of generating radicals (**I**, **II**) under UVA light. These radicals can stabilize by hydrogen transfer from H donor compounds. Perbenzoic acids (**8**) and hydroperoxyacetophenones (**9**) are assumed as intermediates in the formation of benzoic acids (**2**) and phenylglyoxals (**3**). As peroxides they might occur as precursors in the formation of benzoyloxyl radicals as well as in the formation of the even more reactive hydroxyl and oxyl radicals.

With the intention of transferring the photochemical behaviour of dibenzoyl methanes from model solutions to more realistic conditions, we have extended the irradiation medium to commercial emulsions. The results obtained by thin film irradiations show high degradation rates and confirm the photochemistry described. In a forthcoming publication we will give a detailed report about these investigations on dibenzoyl methanes to be incorporated in commercial emulsions and exposed to sunlight.

References

[1] S. Schauder, *Sonnenschutzfilter Göttinger Liste 1991/92*, Deutscher Apotheker Verlag, Stuttgart, 1991.

[2] N.M. Roscher, M.K.O. Lindemann, S.B. Kong, C.G. Cho and P. Jiang, Photodecomposition of several compounds commonly used as sunscreen agents, *J. Photochem. Photobiol. A: Chem.*, *80* (1994) 417–421.

[3] A. Deflandre and G. Lang, Photostability assessment of sunscreens. Benzylidene camphor and dibenzoylmethane derivatives, *Int. J. Cosmet. Sci.*, *10* (1988) 53–62.

[4] K. Hirayama, *Handbook of Ultraviolet and Visible Absorption Spectra of Organic Compounds*, Plenum, New York, 1967.

[5] H. Gonzenbach, T.J. Hill and T.G. Truscott, The triplet energy levels of UVA and UVB sunscreens, *J. Photochem. Photobiol. B: Biol.*, *16* (1992) 377–379.