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A Tetramethoxybenzophenone as Efficient Triplet Photocatalyst for the Transformation of Diazo Compounds

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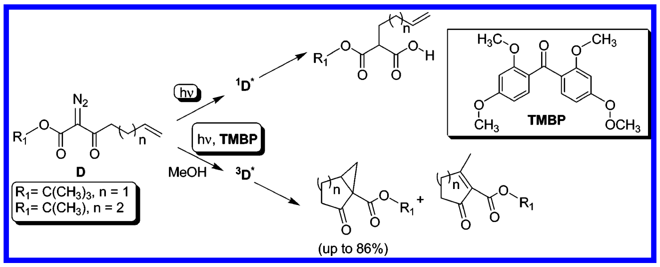
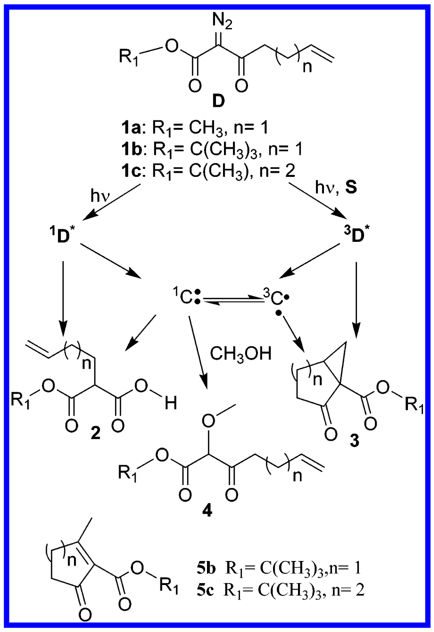


The aromatic ketone 2,2′,4,4′-tetramethoxybenzophenone has a strong absorption band between 300 and 375 nm, and its π,π^* triplet excited-state is selectively populated in methanol. Both facts make this aromatic ketone a versatile and efficient triplet photocatalyst for the transformation of α-diazo carbonyl compounds into mainly the cyclopropanation product.

α-Diazo carbonyl compounds give the Wolff rearrangement as the paramount reaction pathway under direct irradiation (**2** in Scheme 1).[1] The [1,2] shift that gives rise to ketenes proceeds in the singlet state, accompanying or following the loss of N_2. Thus, upon its excitation, methyl 2-diazo-3-oxoheptenoate (**1a**)[2] leads mainly to the Wolff rearrangement product **2a**. The O−H insertion product **4a** is also detected when using alcohols as reaction media (Scheme 1). By contrast, benzophenone (BP)-mediated photosensitization provides the diazo compound triplet, which minimizes **2a** (→9%) as well as **4a** (→9%) and affords mainly the intramolecular cyclopropanation product **3a** (→88%). It has been stressed that Wolff rearrangement is the major reaction pathway of the singlet carbene, while C═C addition of triplet carbene is fast relative to intersystem crossing.

The triplet-sensitized photolysis of α-diazo carbonyl compounds has been performed in the presence of a high excess of BP.[2,3] But, even so, it is unlikely that complete sensitization is achieved in each case, since it is known the existence of diazoalkane transitions at longer wavelengths than those of BP.[4] Moreover, due to its $n\pi^*$ nature, the BP triplet easily abstracts hydrogen from the solvent, which results in the photosensitizer transformation into BP-derived alcohols and pinacols.[5] Both facts prevent the use of BP as an efficient triplet photocatalyst for diazo compounds transformation.

SCHEME 1. Reaction Pathways for the Transformation of Alkyl 2-Diazo-3-oxoalkenoates



Previous studies have shown that after substitution of electron-donating groups, such as OCH_3, onto the aromatic rings of BP the relative position of $n\pi^*$ and $\pi\pi^*$ triplet states is largely affected by the solvent polarity. Thus, in the case of 4-metoxybenzophenone (MBP), while its triplet has an n,π^* configuration in the nonpolar cyclohexane, the π,π^* triplet predominates in aqueous solutions.[6] Transient absorption spectra due to n,π^* and π,π^* being simultaneously populated are observed upon laser excitation in polar solvents such as acetonitrile.[7]

Therefore, in principle, it could be possible to obtain a selective π,π^* triplet population in media less polar than aqueous solutions by attaching a higher number of electron-donating groups to the aromatic rings of BP, such as in the case of 2,2′,4,4′-tetramethoxybenzophenone, TMBP.[8]

We report here that it is possible to selectively populate the π,π^* triplet of TMBP in methanol. Both the lower capability of π,π^* triplets for direct hydrogen abstraction and the much stronger absorption of TMBP than BP at wavelengths longer

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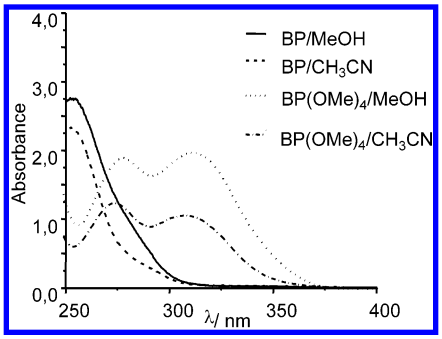

FIGURE 1. UV/vis absorption spectra of BP and TMBP in CH_3CN and MeOH. Sample concentration was 10^{-4} M.

TABLE 1. Photophysical Properties of TMBP[a]

	CH_3OH	CH_3CN	dioxane
λ_{abs} (nm)	311	308	307
λ_{em} (nm)	480	448	453
Φ_f[b]	0.004	0.005	0.004
${}^1\tau$[c] (ns)	1.4	2.0	2.5
E_S (kcal·mol^{-1})	75	76	78

[a] Parameters: absorption maximum of the longest π,π^* transition (λ_{abs}), emission maximum (λ_{em}) at $\lambda_{exc} = 355$ nm, fluorescence quantum yield (Φ_f), singlet lifetime (${}^1\tau$), and energy of the singlet excited state (E_S). [b] Fluorescence quantum yields at $\lambda_{exc} = 355$ nm were determined using quinine bisulfate (0.5 M) in sulfuric acid as described elsewhere.[17] [c] Based on the fluorescence decay monitored at 470 nm.

than 300 nm (see below) prompted us to study the versatility of TMBP as photocatalyst for the transformation of diazo compounds.

The photochemical and photophysical properties of TMBP were studied by means of time-resolved measurements. Its capability as photocatalyst for diazo compound transformation was tested in two model compounds, *tert*-butyl 2-diazo-3-oxo-6-heptenoate (**1b**) and *tert*-butyl 2-diazo-3-oxo-7-octenoate (**1c**), using acetonitrile and methanol as polar solvents. For comparison purposes, the studies were also performed with BP.

Figure 1 shows the absorption spectra of TMBP in acetonitrile and methanol. It exhibits two strong bands at $\lambda_{max} = 278$ nm ($\log \epsilon = 4.45$) and 312 nm ($\log \epsilon = 4.42$) in methanol, plus a long tail in the lowest energy region.[9] The maximum at 312 nm could be assigned to the 2,4-dimethoxybenzoyl chromophore, by comparison with absorption spectra of substituted benzophenones.[10] That maximum undergoes a small hypsochromic displacement in less polar solvents (from 312 nm in methanol to 307 nm in dioxane), which is in agreement with the π,π^* character of this electronic transition (Table 1). Similarly to the analogous BP transition with maximum at 253 nm in methanol, it displays a hyperchromic effect in the proton-donating solvent (compare methanol vs acetonitrile in Figure 1). On the other hand, the absorption at longer wavelengths, partially overlapped by the high-intensity band at 312 nm, can be assigned to the carbonyl n,π^* transition. Overall, TMBP has a much higher molar extinction coefficient than BP in the 300−375 nm wavelength range (Figure 1).[9]

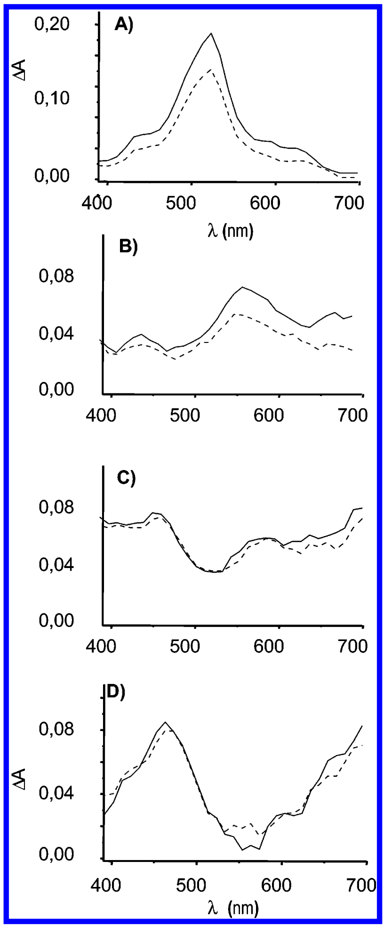

FIGURE 2. Triplet−triplet transient absorption spectra of (A) BP in CH_3CN, (B) TMBP in cyclohexane, (C) TMBP in CH_3CN, and (D) TMBP in MeOH. Spectra A were taken 40 (—) and 400 ns (--) after the laser pulse ($\lambda_{exc} = 355$ nm). Spectra B−D were taken 10 (—) and 70 ns (--) after the laser pulse ($\lambda_{exc} = 355$ nm).

TMBP shows very small fluorescence in different solvents (Table 1, Figure S1 in the Supporting Information). The emission maximum is located at 480 nm in methanol but moves to ca. 450 nm in other solvents. Fluorescence lifetime (${}^1\tau$) and quantum yield (Φ_f) are similar for all the solvents, with values in the range of 1.4−2.5 ns and 0.004−0.005, respectively. The excitation spectra (λ_{em}= emission maximum) shows that the emission band is not related to the strong absorption at λ_{max}= 310 nm (of π,π^* nature) but to a weak absorption located at ca. 350 nm, partially overlapped by the high-intensity π,π^* band (Figure S1). This absorption can be safely assigned to the n,π^* transition by comparison with that of BP (maximum at 340 nm in methanol). The intersection between the normalized emission and excitation traces allowed us to locate the 0−0 transition and to estimate the singlet excited-state energy (E_S); see Table 1. The lowest value was found in methanol, which could indicate the stabilization of this excited state by solvation and/or formation of a hydrogen-bonded complex in the hydrogen-bond-forming solvent.

For deactivation of the S_1 singlet excited state, one route is via intersystem crossing. In order to detect the TMBP T−T absorption, laser flash photolysis (LFP) experiments were carried out on solutions of TMBP in cyclohexane, methanol, and acetonitrile, employing a 355 nm laser as the excitation source. For comparison, the typical spectrum of benzophenone triplet (n,π^* nature) is also included (Figure 2A). In methanol, the transient absorption bands of TMBP are located at $\lambda_{max} = 470$ nm and close to 700 nm (Figure 2D). These absorptions could be assigned to the ^{3}TMBP of π,π^* character by similarity with

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TABLE 2. Photocatalytic Studies.

run	D	S	S/D molar ratio	λ [a]	solvent	ratio[d] (%)		
						2	**3**	**5**
1	**1b**			A	CH_3CN	83	17	
2	**1b**			B	CH_3CN	87	13	
3	**1b**			A	CH_3OH[b]	64	20	
4	**1b**	BP[c]	0.10	A	CH_3CN	64	36	
5	**1b**	TMBP[c]	0.10	A	CH_3CN	4	90	6
6	**1b**	TMBP[c]	0.10	B	CH_3CN	17	70	13
7	**1b**	TMBP[c]	0.10	C	CH_3CN	16	70	14
8	**1b**	TMBP	0.25	B	CH_3OH	0	65	35
9	**1b**	TMBP	0.50	B	CH_3OH	0	73	27
10	**1b**	TMBP	1.00	B	CH_3OH	0	86	14
11	**1c**			A	CH_3CN	93	7	
12	**1c**	BP[c]	0.10	A	CH_3CN	43	38	19
13	**1c**	TMBP[c]	0.10	A	CH_3CN	18	66	15
14	**1c**	TMBP[c]	0.10	B	CH_3CN	24	70	6
15	**1c**	TMBP[c]	0.10	C	CH_3CN	25	69	6
16	**1c**	BP[b,c]	0.05	B	CH_3OH	39	36	12
17	**1c**	TMBP[b]	0.10	B	CH_3OH	17	71	4
18	**1c**	TMBP[b]	0.05	B	CH_3OH	26	60	4

[a] Deaerated solutions irradiated for 5 h. Excitation: A, $\lambda > 300$ nm; B, $400 < \lambda < 320$ nm; C, $\lambda > 350$ nm. [b] Compound **4** is formed in ≤10%. [c] Important photochemical degradation of the sensitizer is observed. [d] Isolated yields are reported in the Experimental Section (see SMI).

those of MBP in acetonitrile–water mixtures.[6,11] The spectra obtained in cyclohexane show the presence of a new band located at $\lambda_{max} = 580$ nm (Figure 2B), which could be ascribed to the ^{3}TMBP with n,π* nature[6,11] (compare with Figure 2A for BP).

In acetonitrile, transient absorption spectra due to n,π * and π,π* being simultaneously populated are observed upon laser excitation (Figure 2C). These results demonstrate that a higher number of electron-donating groups on the aromatic rings of the TMBP provokes a better proximity of the two lowest triplet states, and a small π,π* triplet population is observed even in a low polar solvent such as cyclohexane.

The capability of TMBP to act as triplet photocatalyst was tested in the transformation of diazo compounds **1b** and **1c**. The influence of the sensitizer/diazo (*S*/*D*) molar ratio, the use of either acetonitrile or methanol as solvent, and the excitation wavelengths ($\lambda > 300$ nm, $400 > \lambda > 320$ nm, and $\lambda > 350$ nm) was explored (Table 2). The deaerated solutions were irradiated for 5 h in the presence and in the absence of the aromatic ketone.

In both solvents, the direct photolysis ($\lambda > 300$ nm [12] or $400 > \lambda > 320$ nm) of **1b** leads mainly to **2b** (runs 1–3). The intramolecular addition to the double bond is a minor reaction (**3b** → 20%). In methanol, formation of the O–H insertion product is also detected (run 3). On the other hand, the cyclopropanation yield increases after excitation at $\lambda > 300$ nm in the presence of a small amount of BP (BP/**1b** = 0.1), though **2b** still predominates (run 4).

As mentioned above, a drawback of using BP as photocatalyst is its important photochemical degradation by reaction with the solvent. In fact, analysis of the photolyzate by NMR revealed an important degradation due to the n,π* nature of the BP low-lying triplet excited state. Interestingly enough, under the same conditions, the TMBP-photosensitized transformation of **1b** mainly affords the cyclopropanation product (90%), accompanied by a small amount of a new compound, unsaturated ketone **5b** (run 5).[13] An appreciable degradation of the photosensitizer is also observed in this case. Results are wavelength-dependent, as shown by an enhanced yield of **2b** and **5b** combined with a decrease of the cyclopropanation product yield when exciting at $400 > \lambda > 320$ and $\lambda > 350$ nm (compare runs 5–7). In addition, the product distribution changes with the solvent and the *S*/*D* molar ratio; thus, **2b** is not detected in methanol and the **3b**/**5b** ratio increases with the photosensitizer concentration (compare run 6 with runs 8–10).

Similar studies were performed with diazo compound **1c**. Direct irradiation of **1c** leads also mainly to the Wolff rearrangement product (93%, run 11). Results for the photosensitized reactions are analogous to those for **1b**; cyclopropanation is the main process when using TMBP (runs 12–15, 17, and 18). It is remarkable that compound **3c** is the major product even when using a TMBP/**1c** molar ratio of 0.05 (compare runs 17 and 18). In good agreement with LFP experiments, insignificant photochemical degradation of the TMBP is observed in methanol;[14] meanwhile important decomposition is detected for TMBP in acetonitrile and for BP in both solvents. As shown above, the product distribution was affected by the wavelength, the solvent, and the photosensitizer concentration. As these findings could indicate secondary photoreactions of primary products, control experiments were performed to determine the photostability of **3** to direct or photosensitized irradiation. However, no new products are detected in either case. For example, **3b** and **3c** do not undergo any transformation after direct irradiation at $400 > \lambda > 320$ nm (CH_3CN, 5 h). Under the same conditions, TMBP does not photosensitize the transformation of **3c**.

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[12] Pyrex filtered. Lamp with a broad emission band between 280 and 380 nm ($\lambda_{max} = 320$ nm). Other sharp emissions are ca. 400, 440, and 540 nm.

[13] The formation of these types of products in BP-photosensitized transformation of diazo compounds has not been previously reported. The structure of **5b** was assigned by comparison with **5a**, which has been synthesized (in a 55% yield) by Pd(II)-mediated cyclization of **1a** (Taber, D. F.; Amedio, J. C., Jr.; Sherrill, R. G. *J. Org. Chem.* **1986**, *51*, 3382). No similar studies have been done for **1b**,**c**.

[14] It has been reported that, upon photoexcitation of TMBP in methanol, a transient absorption attributed to ketyl radical is observed.[8] However, lamp irradiation of this ketone in methanol revealed its photostability (less than 5% of decomposition, 2 h of irradiation).

Analysis of the data summarized in Table 2 reveals that both **3b**/**3c** and **5b**/**5c** [15] are formed in the triplet-sensitized processes. Therefore, the presence of **3** upon direct photolysis could agree with spin equilibration of the carbene, which would allow generating the triplet carbene and leading to the cyclopropanation product. Meanwhile, the absence of **5** in the direct photolysis of **1** could be due to the low efficient intersystem crossing yielding the diazo triplet excited state. However, since formation of **5** is enhanced when decreasing the photosensitizer concentration (compare runs 8−10), it must be obtained upon direct excitation of its precursor,[16] which should arise from the diazo triplet excited state. It also should be noted that irradiation of compound **3** either in the presence or in the absence of a catalytic amount of TMBP does not afford the cyclic enone **5**. Finally, a TMBP/**1b** molar ratio of 0.25 is enough to avoid direct diazo compound irradiation, as shown by the absence of **2b** under such conditions (run 8).

In summary, experimental data indicate that it is possible to selectively populate the π,π^* triplet of TMBP in methanol. Its low capability for direct hydrogen abstraction from methanol together with the strong absorption band of TMBP (300−375 nm range) make this aromatic ketone a versatile and efficient triplet photocatalyst for diazo compounds transformation in such a polar solvent. In addition, 2-methyl-5-oxocycloalk-1-enecarboxylates are generated (up to 35% yield) in the triplet-photosensitized transformation. The present study offers useful guidelines for the design of aromatic ketones with the desirable photophysical characteristics to act as cheap triplet photocatalysts.

Experimental Section

Preparation of *tert*-Butyl 2-Diazo-3-oxohept-6-enoate (1b). General Procedure. Mesyl azide[18] (1.24 g, 9.28 mmol) and triethylamine (1.40 mL, 19.0 mmol) were added to a solution of *tert*-butyl 3-oxohept-6-enoate (2 g, 10.31 mmol), prepared by the method of Weiler,[19] in 20 mL of acetonitrile. After stirring for 3 h at room temperature, 10 mL of 10% aqueous NaOH (10 mL) was added and the product was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by chromatography on silica gel with hexane/ethyl acetate (15:1) as the eluent to give 1.79 g (80%) of pure **1b** as yellow oil. R_f (hexane/EtOAc, 1:1) 0.81. ^1H NMR (300 MHz, $CDCl_3$) δ 5.74−5.89 (m, 1H), 4.95−5.07 (m, 2H), 2.91 (t, $J = 9$ Hz, 2H), 2.33−2.40 (m, 2H), 1.51 (s, 9H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 192.5, 160.5, 137.0, 115.3, 83.1, 50.9, 39.3, 28.2, 28.1.

Photosensitized Transformation of *tert*-Butyl 2-Diazo-3-oxohept-6-enoate (1b). General Procedure. To a solution of *tert*-butyl 2-diazo-3-oxo-6-heptenoate (300 mg, 1.32 mmol) dissolved in deaerated CH_3CN, $BP(OMe)_4$ (42 mg, 0.13 mmol) was added, and the solution was irradiated for 5 h. The solvent was evaporated under vacuum, and the crude product was purified by chromatography on silica gel with hexane/ethyl acetate (15:1) as the eluent to yield a mixture of 234 mg (90%) of **3b** as yellow oil and 30 mg (6%) of **5b** as yellow oil. *cis*-*tert*-Butyl 2-oxo-bicyclo[3.1.0]hexane-1-carboxylate (**3b**): R_f (hexane/EtOAc, 3:1) 0.47. ^1H NMR (400 MHz, $CDCl_3$) δ 2.43−2.48 (m, 1H), 2.09−2.17 (m, 3H), 1.87−1.91 (m, 2H), 1.55 (s, 9H), 1.22 (t, $J = 4$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3, 166.2, 80.5, 37.2, 32.7, 31.4, 27.0, 20.7, 19.8. MS EI (*m/z*) 196 (M^+, 25), 181 (100), 161 (5). IR (film, cm^{-1}) 2978, 1739, 1712, 1369, 1324, 1305, 1272, 1158, 1032. *tert*-Butyl 2-methyl-5-oxocyclopent-1-enecarboxylate (**5b**):R_f (hexane/EtOAc, 3:1) 0.28. ^1H NMR (400 MHz, $CDCl_3$) δ 2.58−2.60 (m, 2H), 2.40−2.43 (m, 2H), 2.31 (s, 3H), 1.52 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.7, 181.9, 162.5, 134.0, 81.8, 34.9, 32.4, 28.2, 19.1. MS EI (*m/z*) = 196 (M^+, 2), 181 (3), 141 (100). IR (film, cm^{-1}) 2977, 2925, 1738, 1705, 1633, 1368, 1354, 1254, 1251.

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Supporting Information Available: Synthesis and characterization data and NMR spectra for compounds **1b**,**c**, **2b**,**c**, **3b**,**c**, and **5b,c**, UV/vis spectra of **1b** and TMBP, and emission and excitation spectra of TMBP. This material is available free of charge via the Internet at http://pubs.acs.org.

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[15] Compound **5c** has been obtained in a 21% yield from 6-methyl-3,4-dihydropyran-2-one: Hird, A. W.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 14988.

[16] Further studies will be pursued to determine the structure of the precursor affording **5**.

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