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# Novel [4 + 2] Cycloaddition between Thiobenzophenone and Aryl-Substituted Alkenes via Photoinduced Electron Transfer

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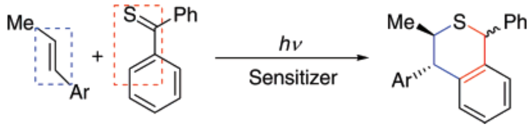
## ABSTRACT



**The [4 + 2] cycloaddition products between thiobenzophenone (1) and arylalkenes (2) were obtained in the presence of (thia)pyrylium salts (sensitizer = 3 or 4) as electron transfer photosensitizers. Although both radical cations $1^{\bullet+}$ and $2^{\bullet+}$ are generated, only the former is involved in the process.**

Although the Diels−Alder (DA) reaction was discovered more than 80 years ago, it still remains one of the most powerful tools in synthetic organic chemistry; its mechanism has also attracted considerable interest from a theoretical point of view.[1] The electron transfer (ET)-mediated DA reaction, where the diene or the dienophile units are in the radical cationic form, has also been intensively investigated.[2]

Likewise, substantial attention has been paid to hetero-DA processes for the synthesis of six-membered heterocycles.[3] Azadienes have been by far the most frequently used synthons for this purpose; however, a number of DA processes with thiadienes have also been reported.[4]

In this context, it was of interest to explore the feasibility of electron-transfer-mediated [4 + 2] cycloaddition reactions between thiadienes and alkenes, a possibility that has not been investigated to date. In order to test this concept, thiobenzophenone (**1**) and arylalkenes (**2**) were chosen as reaction partners and (thia)pyrylium salts **3** and **4** as ET photosensitizer(s).[5] Here, the thiadiene system would be defined by the thiocarbonyl group and one of the double bonds of the phenyl groups. Following this approach, formation of new photoproducts arising from [4 + 2] cycloaddition has been achieved in moderate to high yields. The scope of this reaction was investigated at a preliminary stage by using different types of 4-substituted-$\beta$-methylstyrenes with either electron-withdrawing or electron-releasing

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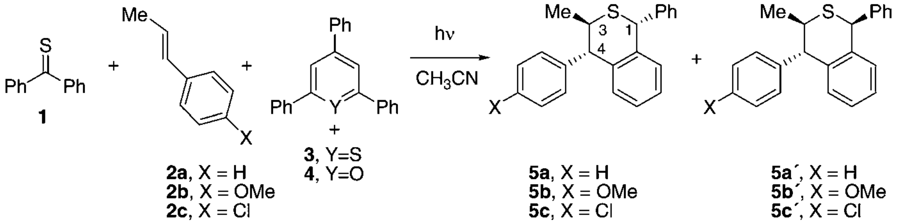
**Scheme 1**



groups. Moreover, laser flash photolysis (LFP) has been employed for elucidation of the reaction mechanism.

In the absence of an ET photosensitizer, the photoreaction between thiobenzophenone and alkenes is known to give [2 + 2] Paterno−Büchi cycloadducts (thietanes).[6] This was confirmed by means of a control experiment, in which irradiation of a mixture of **1** and **2b** in the absence of photosensitizer led to 3-(4-methoxyphenyl)-4-methyl-2,2-diphenylthietane in low yield as the only identifiable photoproduct (see Supporting Information). By contrast, new photoproducts **5** and **5′** were obtained in the present work upon photosensitization with salts **3** and **4** (Scheme 1).

The resulting diastereomeric mixtures were separated by high performance liquid chromatography (HPLC). The structural assignment of the isolated diastereomers was based on their $^1$H NMR and $^{13}$C NMR spectra, using NOESY experiments to establish the relative stereochemistry of the chiral centers. In this context, the interaction between H at position 1 (singlet at $\delta = 5.2-5.4$ ppm) and the methyl group (doublet at $\delta = 1.1-1.2$ ppm), which was found in **5a**−**5c** but not in **5a′**−**5c′**, was particularly useful for diagnostic purposes. The data were consistent with the methyl group at position 3 *trans* to the aryl group at position 4, whereas the two aromatic substituents at positions 1 and 4 could be *cis* (**5**) or *trans* (**5′**). In all cases, the diastereomeric ratio was around 0.9, with a slight excess of the **5′** isomer.

When a mixture of **1** and **2a** was irradiated in the presence of **3**, products **5a** and **5a′** were formed in 90% total yield with a nearly complete consumption of **1** (Table 1, entry 1). Shorter irradiation time and lower concentration of **2a** resulted in improved mass balance and product yields (Table 1, entry 2). Pyrylium salt **4** was found to be less efficient; even after 1 h of irradiation, the conversion of **1** was not complete, and the total yield of both diastereomers dropped to 72% (Table 1, entry 3). In view of these results, the superior thiapyrylium salt **3** was used for all the other preparative experiments.

**Table 1.** Photoinduced Reactions of **1** with 4-Substituted Arylalkenes (**2**) in the Presence of (Thia)pyrylium Salts (**3**/**4**)[a]

| | | | | product yield[d] | |
|---|---|---|---|---|---|
| entry | alkene, concn, sens, time | conv[b] | MB[c] | **5** | **5′** |
| 1 | **2a**, 0.1 M, **3**, 1 h | 99 | 91 | 43 | 47 |
| 2 | **2a**, 0.06 M, **3**, 0.5 h | 100 | 98 | 46 | 52 |
| 3 | **2a**, 0.1 M, **4**, 1 h | 90 | 82 | 35[e] | 37[e] |
| 4 | **2b**, 0.1 M, **3**, 1 h | 92 | 90 | 37 | 45 |
| 5 | **2c**, 0.06 M, **3**, 0.5 h | 100 | 87 | 35[f] | 52[f] |
| 6 | **2a**, 0.06 M, **3**, 0.25 h | 77 | 88 | 31 | 34 |
| 7 | **2b**, 0.06 M, **3**, 0.25 h | 44 | 88 | 15 | 17 |
| 8 | **2c**, 0.06 M, **3**, 0.25 h | 80 | 82 | 30 | 32 |
| 9 | **2a/2b**,0.06 M, **3**, 0.25 h | 41 | 79 | | |
| 10 | **2a/2c**, 0.06 M, **3**, 0.25 h | 60 | 81 | | |

[a] **1**: 0.05 M, **3** or **4**: 0.005 M in CH$_3$CN under nitrogen atmosphere, irradiated with a high-pressure mercury lamp at room temperature (effective irradiation wavelength between 280 and 500 nm). [b] Calculated with the recovered **1** or PhCOPh. [c] Mass balance. [d] Determined by GC analysis using PhSSPh as internal standard, error <5%. [e] Isolated yields: 29% (**5a**) and 36% (**5a′**). [f] Isolated yields.

The presence of an electron donor group as in *trans*-anethole (**2b**) was associated with a slight decrease in the yield of both photoproducts **5b** and **5b′**; besides, longer irradiation time was required for a good conversion (Table 1, entry 4). In the case of 4-chloro-*trans*-$\beta$-methylstyrene (**2c**), no clear effect was observed (Table 1, entry 5), indicating that electron-withdrawing groups do not significantly affect the reaction. The overall reactivity of **2a**, **2b**, and **2c** with **1** under oxidative electron transfer conditions, determined at short irradiation times, followed the order **2c** ≥ **2a** > **2b** (Table 1, entries 6−8). This reactivity order seems contrary to expectations if the reaction is assumed to occur via the alkene radical cation, suggesting the involvement of thiobenzophenone as donor in the productive electron transfer pathway.

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In order to better understand the substituent effects, competitive experiments were performed. Thus, when a mixture of **1** with **2a** and **2b** was irradiated in the presence of **3** (Table 1, entry 9), the ratio **5b+5b′/5a+5a′** was ca. 2.25/1; in other words, **2b** was found to be markedly more reactive than **2a** toward $\mathbf{1}^{\bullet+}$. On the other hand, a similar experiment using a mixture of **1** with **2a** and **2c** (Table 1, entry 10) led to a **5c+5c′/5a+5a′** ratio of only 0.55/1, showing that **2c** is the least reactive of the arylalkenes toward $\mathbf{1}^{\bullet+}$. Thus, under conditions where the same amount of thiobenzophenone radical cation was generated, the reactivity order was actually **2b** > **2a** > **2c**, as expected from the relative nucleophilicity of the arylalkenes.

**Table 2.** Thermodynamics and Kinetics of the ET Reaction from the Triplet Excited State of **3** in $CH_3CN$ at 20 °C

| $Q^a$ | $E_{ox}{}^b$ | $\Delta G_{ET}{}^c$ | $10^{-10}\ k_q{}^d$ |
|---|---|---|---|
| **1** | nd | nd | 2.3 |
| **2a** | 1.7 | −10.3 | 1.6 |
| **2b** | 1.2 | −17.2 | 2.1 |
| **2c** | 1.7 | −7.9 | 1.7 |

[a] Quencher. [b] Oxidation potential given in V, from ref 7. [c] For ET from the excited triplet of **3**, calculated as in ref 8; given in kcal/mol. [d] Rate constant for triplet quenching ($k_q$) in $M^{-1}\ s^{-1}$.

As mentioned above, thietanes are formed in the absence of photosensitizer by a [2 + 2] process involving the triplet excited state of **1** and the neutral arylalkene.[6] Electron transfer photosensitization completely changes the course of the reaction, being essential for the formation of [4 + 2] cycloadducts. Thus, the photosensitizer acts as a one electron-oxidizing agent rather than a triplet energy donor.

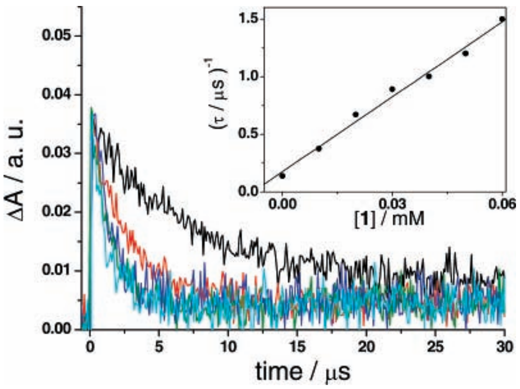

**Figure 1.** Decay traces of the T−T absorption of **3** (0.03 mM) measured at 460 nm in the presence of increasing amounts of **1**: 0 M (black), 0.01 mM (red), 0.02 mM (green), 0.03 mM (blue), 0.04 mM (aqua). Inset: Plot of $1/\tau$ against concentration of **1** to obtain $k_q(T_1)$.

Owing to the high intersystem crossing quantum yield of **3** ($\Phi_{isc} = 0.94$),[5] its lowest-lying triplet appears to be the most likely excited state involved in the process. Therefore, in order to gain a better understanding of the reaction mechanism and the role of the photosensitizer, triplet quenching of **3** by **1** and the alkene derivatives was investigated by means of laser flash photolysis (LFP).

The results are shown in Table 2. From these data, it became clear that triplet quenching occurs at a near diffusion-controlled rate in all cases.

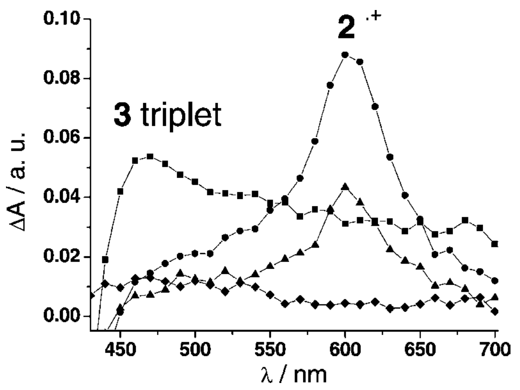

**Figure 2.** Transient absorption spectra obtained upon LFP ($\lambda$ = 355 nm) of **3** (0.06 mM), in acetonitrile, under argon: in the absence of quencher (■) and in the presence of: 1 mM of **2b** (●), 1 mM of **2b** and 0.05 mM of **1** (▲), 0.05 mM of **1** (◆). Spectra recorded 1 $\mu$s after the laser pulse.

**Scheme 2**

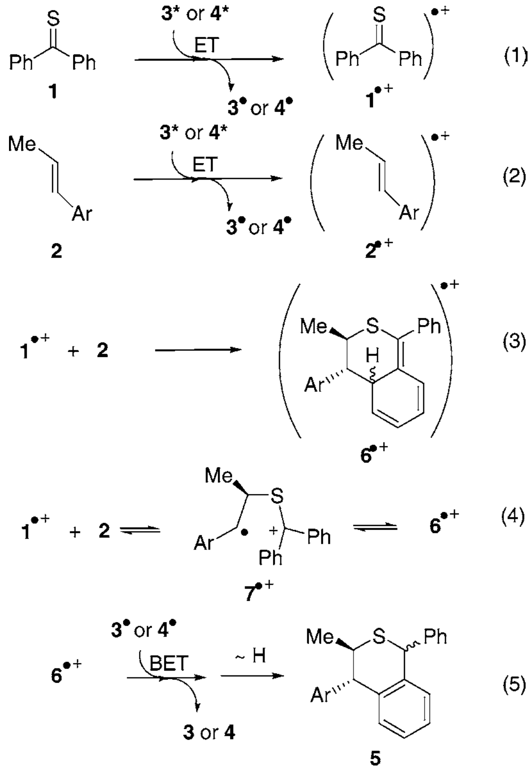

Figure 1 shows the decay traces obtained for the T−T absorption of **3** in the presence of increasing amounts of **1**. Similar effects were observed for the quenching of excited **3** by **2a**−**2c** (not shown).

Moreover, the values of $\Delta G_{\mathrm{ET}}$ (estimated by means of the Weller equation, using the known oxidation potentials of the arylalkenes)[7,8] indicated that ET from the triplet excited state of **3** would be exergonic for all combinations. After the triplet quenching of **3**, no transient species were detected for **1**, **2a**, and **2c**, probably because these species are not compatible with the available time and/or wavelength window. By contrast, in the case of **2b**, the characteristic radical cation absorption was observed, confirming the ET nature of the quenching process (Figure 2).

The proposed reaction mechanism for this novel ET cycloaddition reaction is outlined in Scheme 2. Both the radical cations of **1** and **2a**−**2c** would be generated by ET from the excited triplet state of **3** or **4** (Scheme 2, reactions 1 and 2), but only $\mathbf{1}^{\bullet+}$ would be effective. Its addition to the neutral arylalkene, in a concerted or stepwise fashion, would give rise to radical cation $\mathbf{6}^{\bullet+}$ (Scheme 2, reactions 3 and 4). Back electron transfer (BET) to the pyranyl radical with recovery of the photosensitizer, followed by [1,3] hydrogen migration, would explain formation of the obtained cycloadducts (Scheme 2, reaction 5).

In an attempt to obtain additional experimental support in favor of the proposed mechanism, excitation of **4** in the presence of **1** and **2a** was performed by LFP (see Supporting Information). A new transient absorption band appeared at 550 nm, corresponding to the pyranyl radical. As this is the species arising from reduction of the photosensitizer, its detection provides additional support for the ET nature of the involved process.

In summary, the present work reports a novel electron-transfer-mediated [4 + 2] cycloaddition between a thiadiene and a series of arylalkenes, using (thia)pyrylium salts as photosensitizers. Further mechanistic aspects, scope, and limitations of this reaction are currently under study.

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**Supporting Information Available:** General methods, $^{1}$H NMR and $^{13}$C NMR spectra of **5a**−**5c**, **5a′**−**5c′**, and 3-(4-methoxyphenyl)-4-methyl-2,2-diphenylthietane; transient absorption spectrum obtained after LFP of a mixture of **1**, **4**, and **2a**, as well as decay traces at 550 and 520 nm. This material is available free of charge via the Internet at http://pubs.acs.org.

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