Photocycloaddition of 2-Benzoylthiophene to Methylmaleic Anhydrides

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Summary. Upon direct irradiation with light of wavelengths greater than 300 nm, 2-benzoylthiophene undergoes [2 + 2] cycloadditions with *mono-* and *di-*methylmaleic anhydrides involving the C=C bond of the latter and the benzoyl-substituted thiophene C=C bond.

Keywords. 2-Benzoylthiophene; Photocycloaddition; Methylmaleic anhydrides

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Zusammenfassung. Aus 2-Benzoylthiophen entstehen unter direkter Bestrahlung mit Licht von Wellenlängen > 300 nm in Anwesenheit von Methylmaleinsäureanhydriden [2 + 2]-Cycloaddukte. Die Photoreaktion erfolgt an den C=C-Bindungen des Thiophenrings und des Anhydrids.

Introduction

Photocycloadditions of maleic anhydride derivatives to heterocyclic systems in photosensitized reactions have been one of the research interests of this laboratory [1–8]. Thus, in the course of several investigations concerning photoadditions of citraconic anhydride and 2,3-dimethylmaleimide to furan and of citraconic and 2,3-dimethylmaleic anhydride to several thiophene and benzo[b]thiophene derivatives sensitized by benzophenone, the corresponding [2 + 2] cycloaddition products have been isolated (Fig. 1, [1–5]).

It was possible to isolate the isomeric oxetanes shown in Fig. 2 when 2-benzoylthiophene was irradiated with UV light in the presence of furan, 2-methylfuran, and 2,5-dimethylthiophene [9].

Furthermore, *Cantrell* [10] has found that irradiation of 2-benzoylthiophene in an excess of isobutene results in [2 + 2] cycloaddition of the olefin to one of the double bonds of the thiophene ring as shown in Fig. 3. This can be explained by the fact that the mode of excitation of 2-benzoylthiophene is probably of the π, π^* type [10].

It should also be pointed out that some ketones are capable of adding to the double bond of maleic anhydride as was reported by *Turro* and *Wriede* [11] who

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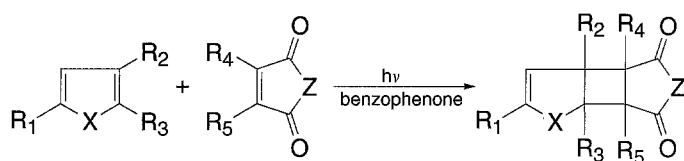† Present Address: INTEVEP, Los Teques, Venezuela

Fig. 1. $X = 0$, S; $Z = 0$, NH; $R' = CH_3$ or H

Fig. 2

3   **Fig. 3**
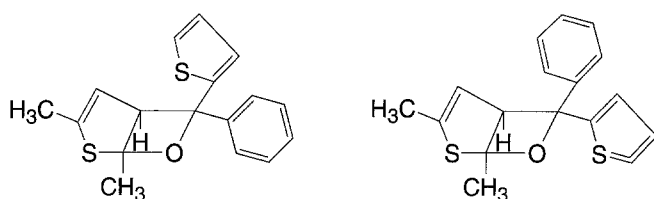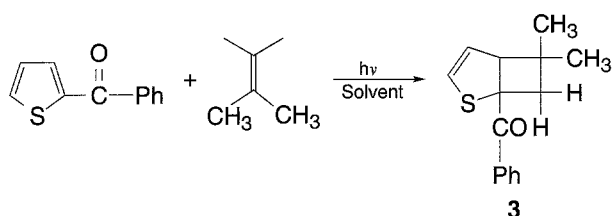
isolated an oxetane when acetone was irradiated in the presence of the anhydride. Some authors suggested that in carbonyl compounds with π, π^* excitation capability, oxetane formation, though inefficient, may be a reaction of the $S_1(n, \pi^*)$ state [12]. Excited 2-benzoylthiophene could as well act as a sensitizer of the anhydrides leading to dimerization reactions.

Finally, there was the question as to whether benzophenone would be needed as the sensitizer or if 2-benzoylthiophene would act as its own sensitizer.

In view of all these facts and queries, it appeared interesting to investigate the photochemical behaviour of 2-benzoylthiophene in the presence of citraconic and 2,3-dimethylmaleic anhydride.

Results and Discussion

First of all, it was found that the use of benzophenone as a sensitizer was not necessary. Thus, the direct [2 + 2] photoaddition of 2-benzoylthiophene to citraconic and 2,3-dimethylmaleic anhydride was achieved by irradiating solutions of 2-benzoylthiophene in dichloromethane in the presence of the corresponding anhydride at wavelengths longer than 300 nm.

After irradiation and work of the crude reaction mixture, two products were isolated for each of the anhydrides. The photoreaction with citraconic anhydride yielded two products (**4, 5**) which after chromatographic separation were identified by NMR, IR and mass spectroscopic analysis as the two isomers depicted in Fig. 4.

The photoreaction with 2,3-dimethylmaleic anhydride gave two products as well as illustrated in Fig. 6. One of them was the photoadduct of 2-benzoylthiophene with
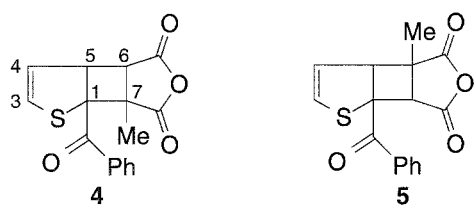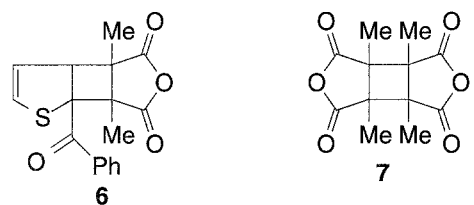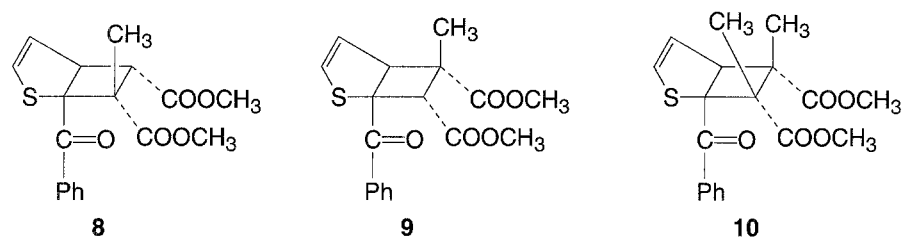
Fig. 4

Fig. 5

Fig. 6

2,3-dimethylmaleic anhydride (6); the other one was the dimer of the anhydride (7). No oxetanes were detected in these reactions.

Due to the fact that the photoproducts are very unstable, being easily hydrolyzed in the presence of moisture, the final product consisted of a mixture of diacid and anhydride. Therefore, the irradiation product was hydrolyzed with base and esterified with diazomethane to afford more convenient compounds for spectroscopic and elemental analyses.

Since the structure of the adducts obtained from citraconic anhydride had to be chosen from a variety of other possible structures, a detailed study based on nuclear *Overhauser* effect analysis (NOE) was carried out on the methyl esters obtained from the hydrolysis and subsequent esterification of the anhydride photoproducts.

On the other hand, the stereochemistry of the adducts could be described on the basis of an analogy to that proposed before for adducts with the same carbon skeleton which had been elucidated by means of selective $^{13}C\{^1H\}$ NOE experiments [13]. The NOE studies of the present investigation were also useful in this connection.The products obtained from all [2 + 2] photocycloaddition reactions studied here have *anti* configuration (Fig. 6).

As stated in the before, 2-benzoylthiophene is capable of yielding oxetanes in the presence of heterocyclic systems such as furan and 2,5-dimethylthiophene as well as undergoing direct [2 + 2] photocycloaddition reactions at one of the double bonds of a heteroaromic nucleus, acting in this case as its own sensitizer. To explain its behavior in [2 + 2] cycloaddition reactions, it has been suggested that 2-benzoyl-thiophene undergoes a π, π^* excitation as mentioned above.

To rationalize the experimental results, it should be pointed out that the triplet energy (T_1) for 2-benzoylthiophene has been reported as 265 kJ/mol [14] above its ground state. This value is significantly lower than that of benzophenone or thiophene whose T_1s amount to about 288 kJ/mol; this implies that in 2-benzoyl-thiophene the excitation is mainly associated with the heterocyclic moiety. In other words, similarly to what happens in 2-acetonaphthone [12], there is an intramolecular energy transfer, and the excitation energy, instead of being localized in the carbonyl group, it is delocalized over the entire system involving the heterocyclic nucleus. This may serve as a rationale to explain the [2 + 2] cycloadditions to the heteroaromatic nucleus. It should also be pointed out that the triplet life time of compounds possessing $T_1(\pi, \pi^*)$ states is commonly found to be much longer than that of compounds with $T_1(n, \pi^*)$ states. This effect presumably counterbalances the low reactivity of these states. As a result, it is also possible to obtain oxetanes, though in a more inefficient way than with compounds possessing n, π^* states.

Regarding the stereo and regio selectivity of these reactions it is worth noting that in contrast to 2-methylthiophene, where the anhydrides add to the unsub-stituted double bond in the ring [4], in 2-benzoylthiophene the [2 + 2] cycloaddi-tion to the heteroaromatic takes place at the double bond bearing the benzoyl group.

A detailed kinetic study has been carried out to derive a mechanism for the photocycloadditions of methylmaleic anhydrides to thiophene. In that context, thiophene and the maleic anhydrides were subjected to a *Stern-Volmer* analysis of their capability as quenchers of the photoreduction of benzophenone [15]. Further-more, evidence was found for the formation of charge transfer complexes between the maleic anhydrides and thiophene. The equilibrium constants for the system thiophene-maleic anhydride in equilibrium with the complex were measured in order to estimate the concentration of the three species (thiophene, anhydride, and complex) which all three act as energy acceptors. Analogously, it is possible that in the case of 2-benzoylthiophene, exciplexes are also involved in the cycloaddition mechanism.

The possible involvement of exciplexes may answer unequivocally the question of orientation in the cycloaddition process. *Griesbeck* and *Stadtmüller* [16] have devoted a great deal of attention to the problem of the formation of regioisomers in cycloadditions such as the *Paterno-Büchi* reaction, and they suggest that regioselec-tivity could be determined by the preorientation of the substrates which would be presumably influenced by steric and electronic factors as well as by solvent effects.

Regarding the formation of dimers of maleic anhydrides which originate from an energy transfer from 2-benzoylthiophene to the anhydride, the results show that no dimer of citraconic anhydride was detected; only that derived from 2,3-dimethyl-maleic anhydride [17] could be isolated and identified by mass spectrometry.

The reason for not obtaining the dimer of citraconic anhydride may be found in the work of *Boule et al.* [18]. Perhaps the use of a solvent of low complexing ability such as dichloromethane influenced the results. *Boule*'s studies revealed that the more substituted the anhydride the more easily the dimers are formed; thus, the order of increasing reactivity is maleic < citraconic < 2,3-dimethylmaleic anhydride.

Structures with the benzoyl group in position 3 were rejected on the basis that the ^{1}H NMR spectra always revealed the presence of two vinyl protons. The mass

spectra of the products exhibit the fragmentation patterns previously reported for compounds of this type [19]: a main fragmentation yielding the two starting materials, 2-benzoylthiophene and anhydride, followed by the normal fragmentation patterns of each compound as well as a stepwise fragmentation of the adduct which has also been reported [19]. The NMR data reported correspond to the methylesters of the diacids obtained from baisc hydrolysis of the anhydride followed by esterification with diazomethane. The ^{13}C NMR data can be found in Table 1 and include the corresponding diacids of the different esters.

Experimental

Melting points were measured with a Fischer-Johnes apparatus and are uncorrected; IR spectra were obtained on a FT-IR Nicolet DX V 5.07 spectrometer; ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian XL 100 and Bruker AC 300 instruments in CDCl$_3$; TMS was used as an internal standard. Mass spectra were determined with a Carlo-Erba/Kratos MS 25 RFA spectrometer. C,H,S,O analyses were carried out using a Fisons-EA 1108 elemental analyser (Venezuelan Institute for Scientific Research, IVIC); all results were in accordance with calculated values within experimental error.

Benzophenone as well as citraconic and 2,3-dimethylmaleic anhydride and 2-benzoylthiophene were purchased from Aldrich. The liquids were distilled and the solids sublimed or recrystallized before use. Dichloromethane (Aldrich) was dried over anhydrous calcium chloride. Diazomethane was prepared by standard procedures [20]. NMR decoupling experiments were carried out according to previously reported procedures [21].

Photochemical Reactions

A solution of 2-benzoylthiophene (12 g, 0.637 mol) and anhydride (citraconic: 3 ml (0.0318 mol); 2,3-dimethylmaleic: 4 g (0.0381 mol)) in 280 ml of dichloromethane was placed in a reaction vessel. A quartz inmersion well containing a pyrex filter sleeve and a Hanovia 450 W lamp was fitted into it. The reaction mixture was irradiated at 10 °C for 8 hours; nitrogen gas was passed through the solution before and during irradiation. After irradiation, the solvent was distilled off. The work-up was performed as given below.

Citraconic anhydride: The excess anhydride was distilled off; then the crude product submitted to thin layer was chromatography and afterwards to chromatography on a silica-gel column (hexane, ether, ethylacetate). Esterification with diazomethane at 5 °C following standard procedures yielded a mixture of two products (4, 5). By means of column chromatography over silica gel (15% ether in hexane) it is possible to achieve one pure product (4). The second isomer was identified in the mixture by NMR spectroscopy, subtracting the resonances of the pure product. Mass spectra of the mixture and of the pure compound (4) are virtually identical.

2,3-Dimethylmaleic anhydride: After irradiation, the white crystals of the dimer of the anhydride were separated by filtration (m.p.: 380 °C, decomp.) and identified by mass spectrometry. The remaining solvent was evaporated. The subsequent procedure is basically the same as that for citraconic anhydride. The yield of crude product is about 20%. After purification and esterification, the yield is considerably diminished.

Spectroscopic data

1-Benzoyl-6,7-dicarbomethoxy-7-methyl-2-thiabicyclo[3,2,0]hept-3-ene (8)

Oily yellowish liquid with a fruity odor; ^{1}H NMR (CDCl$_3$, 300 MHz, ppm): $\delta = 1.9$ (3 H, 7-CH$_3$), 3.0 (d, 1 H, $J_{6,5} = 8.4$ Hz, H-6), 3.4 (3 H, 6-OCH$_3$), 3.65 (3 H, 7-OCH$_3$), 4.76 (qd, 1 H, $J_{5,6} = 8.4$ Hz,

Table 1. ¹³C NMR data; [a] acetone-d₆ (*TMS*); [b] CDCl₃ (*TMS*); [c] these resonances could be assigned either to carbon atom 12 or 13; [d] aromatic resonances at about 131–135 ppm, benzoyl carbonyl at about 178 ppm

	3	4	5	1	6	7	8	11	9	10	12	13
R = CH₃, R' = R'' = H	130.8[a]	123.2	45.6	58.8	56.4	58.0	20.0	–	177.2	174.0	–	–
R' = CH₃, R = R'' = H	131.2[a]	126.4	51.2	56.6	52.8	53.2	–	22.4	177.0	174.8	–	–
R'' = CH₃, R' = H	129.4[b]	121.4	44.4	58.0	53.3	57.1	19.1	–	174.6	171.9	51.8[c]	51.3
R' = R'' = CH₃, R = H	129.4[b]	124.6	49.6	58.0	57.1	55.3	–	21.9	171.9	172.7	51.8[c]	51.3[c]
R = R' = CH₃, R'' = H	131.7[a]	123.2	51.3	56.8	54.6	54.6	14.2	18.3	177.1	171.1	–	–
R = R' = R'' = CH₃	131.3[b]	122.9	51.0	56.2	54.4	54.5	14.1	18.0	175.9	175.9	51.6[c]	51.8[c]
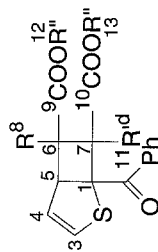
$J_{5,4} = 3.3\,\text{Hz}$, $J_{5,3} = 0.6\,\text{Hz}$, H-5), 5.88 (dd, 1 H, $J_{4,5} = 3.3\,\text{Hz}$, $J_{4,3} = 6.0\,\text{Hz}$, H-4), 6.26 (dd, 1 H, $J_{3,4} = 6.0\,\text{Hz}$, $J_{3,5} = 0.6\,\text{Hz}$, H-3), 7.8 (m, 5-H, aromatic H); NOE data: 7-CH$_3 \rightarrow$ 6 H, 18%; 4 H $\rightarrow$ 5 H, 5%; 3 H $\rightarrow$ 4 H, 10%; $J_{5,6} = 8.4\,\text{Hz}$ confirms trans configuration; no enhancement was observed between 5 H and 6 H; 4 H $\rightarrow$ 6 H, 9%; MS: m/z (%) = 346 (2.36), 315 (1.71), 287 (1.42), 285 (8.82), 255 (4.72), 227 (7.88), 188 (21.57), 181 (4.78), 150 (1.30), 127 (13.73), 123 (4.01), 111 (22.55), 105 (100.00), 99 (2.36), 83 (1.83), 77 (48.04), 59 (11.76); IR: $v = 2950$ (m, COO), 1735 (s, CO), 1680 (m, COOCH$_3$), 1600 (w), 1435 (m), 1270 (s), 1265 (s), 1220 (m), 1160 (m), 1030 (w), 855 (w), 790 (w), 730 (m), 695 (m) cm^{-1}.

1-Benzoyl-6,7-dicarbomethoxy-6-methyl-2-thiabicyclo[3,2,0]hept-3-ene (**9**)

Oily yellowish liquid with fruity odor; ^{1}H NMR (CDCl$_3$, 300 MHz, ppm): $\delta = 1.6$ (s, 3 H, 6-CH$_3$), 3.25 (s, 3 H, 6-methoxy), 3.65 (s, 3 H, 7-methoxy), 3.76 (d, 1 H, $J_{7,5} = 1.2\,\text{Hz}$, H-7), 5.05 (qd, 1 H, $J_{5,7} = 1.2\,\text{Hz}$, $J_{5,4} = 3.6\,\text{Hz}$, $J_{5,3} = 1.2\,\text{Hz}$, H-5), 5.6 (dd, 1 H, $J_{4,5} = 3.6$ Hz, $J_{4,3} = 6$, H-4), 6.4 (dd, 1 H, $J_{3,4} = 6$, $J_{3,5} = 1.2\,\text{Hz}$, H-3); NOE data: 3 H $\rightarrow$ 4 H, 8%; 4 H $\rightarrow$ 5 H, 5%; 6-CH$_3 \rightarrow$ 7 H, 20%; MS: m/z (%) = 346 (1.03), 315 (1.23), 255 (1.85), 227 (3.08), 188 (11.69), 181 (2.05), 150 (1.58), 127 (8.48), 111 (17.43), 105 (100.00), 77 (48.23), 59 (4.3); IR: $v = 2950$ (m, --CO), 1735 (s, --CO), 1680 (m, COOCH$_3$), 1600 (w), 1450 (m), 1270 (s), 1260 (s), 1215 (m), 1155 (m), 1025 (w), 910 (m), 850 (w), 785 (w) 770 (w), 725 (s) 690 (m), 670 (w), 645 (w).

1-Benzoyl-6,7-dicarbomethoxy-6,7-dimethyl-2-thiabicyclo[3,2,0]hept-3-ene (**10**)

^{1}H NMR (CDCl$_3$, 300 MHz, ppm): $\delta = 1.35$ (s, 3 H, 6-CH$_3$), 1.7 (s, 3 H, 7-CH$_3$), 3.3 (s, 3 H, 6-methoxy), 3.55 (s, 3 H, 7-methoxy), 5.05 (d, 1 H, $J_{5,4} = 3.0\,\text{Hz}$, 5-H), 5.65 (dd, 1H, $J_{4,5} = 3.0\,\text{Hz}$, $J_{4,3} = 6.0\,\text{Hz}$, 4-H), 6.4 (d, 1 H, $J_{3,4} = 6.0\,\text{Hz}$, 3-H), 7.8 (m, 5 H, aromatic H); MS: m/z (%) = 361 (1.02), 330 (1.21), 302 (1.80), 243 (2.08), 188 (10.5), 162 (1.65), 105 (100), 83 (1.84), 77 (50.00).

Tetramethylcyclobutane-tetracarboxylic acid dianhydride

MS: m/z (%) = 252 (1.06), 224 (1.63, M$^+$-CO), 208 (1.56, M$^+$-CO$_2$), 180 (11.8, C$_{10}$H$_{12}$O$_3$), 136 (7.2), 126 (1.3, anhydride), 108 (100, tetramethylcyclobutadiene), 93 (19), 54 (16.4, dimethylacetylene) 44 (4.6, CO$_2$), 39 (19), 28 (13.1, CO).

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