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Synthesis of an elusive oxetane by photoaddition of benzophenone to thiophene in the presence of a Lewis acid

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Abstract

It has been possible for the first time to prepare an oxetane by photoaddition of benzophenone to thiophene in presence of BF_3. A photocycloaddition promoted by an electron transfer mechanism is proposed for this reaction.

Keywords: Oxetane; Photocycloaddition; Benzophenone; Thiophene; Boron trifluoride

1. Introduction

In contrast with furan and its methyl derivatives which readily react with excited carbonyl compounds to yield oxetanes [1], thiophene and its methyl derivatives were considered until the late 1960s inert to oxetane formation [2].

Some years ago many attempts carried out to obtain oxetanes from thiophene failed. This behaviour suggested the idea that thiophene was perhaps a good quencher of excited carbonyl compounds. Later, it was found that, in order for the reaction to take place, it was necessary to substitute at least two methyl groups on the heterocyclic ring [3]. Thus 2,5-dimethyl and 2,3-dimethylthiophene turned out to be excellent substrates for excited carbonyl compounds [4]. These results could explain the problem qualitatively since substitution of electron-donating groups to a conjugated diene system should raise its lowest triplet energy level to a higher value above that of the ground state of the unsubstituted diene [5]. Thus, in this case, substitution of one methyl group in the thiophene nucleus raises its lowest triplet energy level closer to that of benzophenone but still not high enough to change it from a quencher to an acceptor of the excited ketone for cycloaddition to take place. Substitution of two methyl groups as in the case 2,5-dimethylthiophene raises the thiophene lowest triplet energy state to a higher level than that of T_1 of benzophenone [6]. The energy transfer then becomes inefficient and the reaction takes place; 2,3-dimethyl thiophene also gives an oxetane, as expected.

This qualitative explanation was later corroborated by correlating inertness to oxetane formation with the quenching activity of these substances on the photoreduction of benzophenone, since the excited state of this compound involved is the same for both types of reaction. In fact, Stern–Volmer plots for thiophene and its monomethyl derivatives indicate that they are good quenchers of excited benzophenone while the dimethyl derivatives are poor quenchers [6]. Even though this explanation based on experimental data satisfies the need to justify the synthetic results, the fact remains that thiophene continues to be an inert substrate for excited carbonyl compounds in oxetane-forming reactions.

In view of this situation, we recently turned our attention to the possibility of carrying out successfully this photocycloaddition reaction by the interaction of a ketone–Lewis acid complex with the heterocycle under consideration in the presence of light.

The following facts prompted us to pursue this method.

(a) It has been shown by nuclear magnetic resonance (NMR) studies that electron-deficient Lewis acids such as BF_2 and BF_3 are capable of forming donor–acceptor complexes with carbonyl compounds [7,8].

(b) It has been reported that the BF_2 complexes in their singlet excited states are a new class of electron acceptors in reaction with alkenes. In these reactions the lowest excited state of the ketonaboron difluoride complexes interact with alkenes by an electron transfer mechanism to give cycloaddition or alkene dimerization products [9]. Furthermore, photolysis of some BF_3–ketone complexes in the presence of cyclic dienes have afforded (2+2) cycloaddition products [10–15].

In the light of these facts, equimolar quantities of thiophene and benzophenone dissolved in dried ether-containing BF_3

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were irradiated. After irradiation and chromatographic separation of the products they were identified as the long-sought oxetane and the corresponding alcohol derived from the opening of the oxetane ring.

2. Experimental details

Melting points (m.p.s) were measured with a Kofler apparatus and are uncorrected. IR spectra were obtained in KBr with a Fourier transform IR Nicolet DX V 5.07 spectrometer. All the ^{1}H NMR, ^{13}C NMR and two-dimensional H, C-correlated (COSY) spectra were recorded on a Brucker Aspect 3000 (300 MHz) instrument. Tetramethylsilane was used as an internal standard and the solvent employed was deuterated chloroform. Mass spectroscopy (MS) was carried out with a Carlo-Erba–Kratos MS25RFA spectrometer. C, H, S, and O analyses were carried out with a Fisons-EA 1108 elemental analyser (Venezuelan Institute of Scientific Research). Benzophenone and boron trifluoride (Aldrich) were used without further purification; thiophene (Aldrich) was used after distillation.

2.1. Photochemical reactions

Equimolar quantities of thiophene (0.01 mole) and benzophenone were dissolved in 10 ml of dried ether containing 0.3 ml of BF_3 and irradiated with a Hanovia 450 W medium pressure lamp. The irradiation was carried out for 5 h at 20 °C under a nitrogen atmosphere in a quartz immersion photoreactor (Applied Photophysics 3230 + 3307). After irradiation, separation and purification of the products were achieved by chromatographing the crude products over silica gel. They were eluted from the column by means of petroleum ether: chloroform (3:1). After the work-up, two products were isolated whose structures were elucidated as follows.

2.2. Products (Scheme 1)

2.2.1. Adduct 1. Yield, 10%; m.p., 68–70 °C, decomposes to adduct **2** (fastest in solution). IR: ν 3088, 2919, 1493 (CH_3), 3060, 1595, 1578, 970 (trimethylene oxide ring), 856, 798 (C=C and Ph) cm^{-1}. MS: m/z (%) 182 (80), 165 (51), 105 (20), 85 (4), 84 (14), 77 (12), 32 (6), 28 (10). This compound is very unstable and decomposes very rapidly to product **2**.

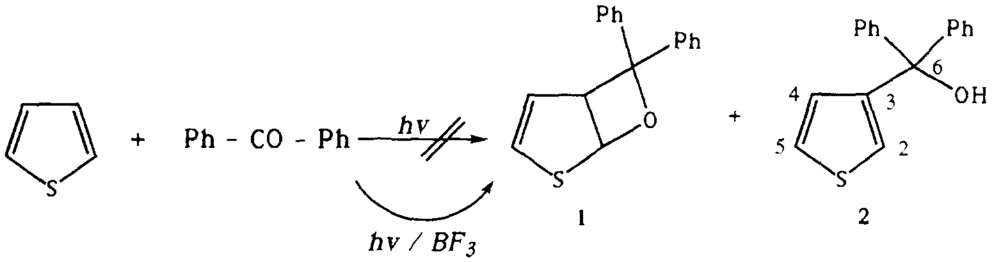
2.2.2. Adduct 2. Yield, 90%; recrystallized from chloroform:petroleum ether (1:2); m.p., 160–162 °C. IR: ν 3627–3300, 1214 (OH and C–O), 3080, 2919, 1494, 1446 (CH_3), 3059, 1594, 1510, 795 (C=C and Ph) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.64 (d, J = 5 Hz, 1H, 2-H), 7.50 (d, J = 9 Hz, 1H, 5-H), 7.21 (m, 10 H, aromatic H), 7.14 (d, J = 9 Hz, 1H, 4-H), 1.60 (s, 1H, –OH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.8 (s, C-3), 143.16 (s, aromatic-C), 137.4 (d, C-4), 131.7 (d, C-5), 131.0 (d, aromatic-CH), 130.8 (d, aromatic-CH), 127.8 (d, aromatic-CH), 127.5 (d, aromatic-CH), 126.6 (d, C-2), 126.0 (d, aromatic-CH), 71.0 (s, C-6) ppm. MS: m/z (%) 183 (30), 166 (40), 165 (12), 106 (20), 105 (24), 83 (4), 85 (23), 77 (15), 32 (4). Anal. Found: C, 76.32; H, 5.14; O, 5.89; S, 11.90. $C_{17}H_{14}OS$ calc.: C, 76.69; H, 5.25; O, 6.00; S, 12.04%.

3. Discussion

Boron trihalide complexes with a variety of organic bases have been studied by spectroscopic methods to evaluate their energetics and structural features. Examples of the organic bases involved in different studies of BF_3 adducts include pyridines, alkylethers, amines, nitriles, sulfides, cyclic ketones, ethers, benzophenone, diethylketone, β-diketones, benzaldehydes, unsaturated alicyclic aldehydes and many other compounds [13]. In most of these studies, thus far found in the literature, the most widely employed techniques are ^{1}H NMR, ^{13}C NMR and ^{19}F NMR. The components were mixed in many instances in a 1:1 mole ratio, as well as in excess of one of the two reagents [13].

These complexes have been useful acting as intermediates in Lewis-acid-catalyzed organic reactions of different types, including (2 + 2) cycloadditions, linear additions and various types of photoreaction.

The initial step in catalysis of these reactions by a Lewis acid appears to be the complexation of the organic compound with the Lewis acid. In the case of ketones and aldehydes it is generally accepted that the bonding takes place through one of the lone pairs of the carbonyl oxygen atom. Subsequently the base which has been activated by complexation and further by light in the case of photoreactions undergoes attack by another reactant present in the reaction medium which could be an olefin or a conjugated system of some kind such as that present in a heterocyclic ring [8]. The structure



Scheme 1.

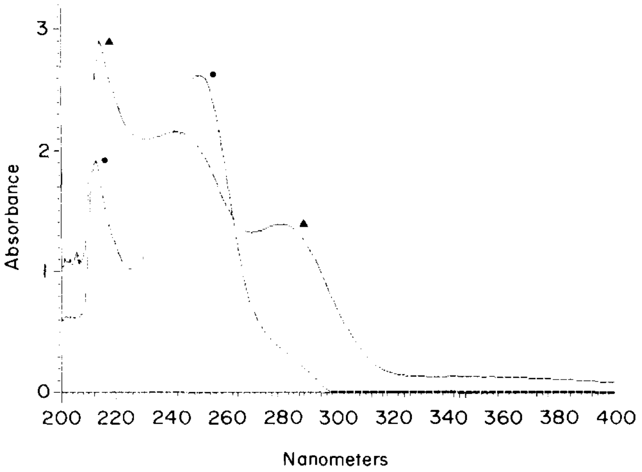


Fig. 1. UV spectra of benzophenone (●) and the benzophenone–BF_3 complex (▲).

and properties of the intermediate complex such as charge distribution should be very important in determining the reactivity, regioselectivity and stereoselectivity in the final product.

The results obtained in the present investigation indicate that the benzophenone–BF_3 complex is capable of reacting with thiophene to yield an unstable oxetane **1** that opens up to yield an alcohol **2** (Scheme 1). Since this seems to be a reasonable description of the course of the reaction it is also reasonable to think that benzophenone–BF_3 complex excited by light leads to an exciplex whose excitation energy is lower than the lowest triplet energy level of thiophene which under the circumstances cannot act as a quencher and then, presumably, the electron-rich heterocycle interacts with the electron-deficient donor base complexed to BF_3. The latter frees itself from the complex and a biradical intermediate precedes the formation of the oxetane or, once the electron transfer from the heterocycle and the separation of BF_3 have taken place, the exciplex formed by the carbonyl compound and the heterocycle collapses to the oxetane.

In this way the UV spectra of both the ketone–BF_3 complex and benzophenone alone were obtained (dry ether) and are shown in Fig. 1. As may be observed from the absorption curves, when BF_3 is added to benzophenone, the n–π^* band of the ketone is shifted from 250 to 280 nm; this may presumably indicate that what has been said in the previous paragraph can be sustained spectroscopically.

The instability of the oxetane formed has perhaps to do with the intrinsic nature of thiophene [6]. Something similar occurs with pyrrole. Thus the early attempts to make oxetanes from pyrroles and imidazoles failed and only alcohols produced by the opening of the oxetane ring were isolated [14,15].

Regarding the regioselectivity of the reaction, it is interesting to note that the final product implies a head-to-head cycloaddition which is consistent with the compounds previously isolated in this laboratory [16]. Other heterocycles which thus far have been shown to be inert to oxetane formation are being investigated in this laboratory by applying the method just described.

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