

Synthesis of Oxetanes by Photoaddition of Carbonyl Compounds to Pyrrole Derivatives

C. Rivas and R. A. Bolívar

Centro de Petróleo y Química, Instituto Venezolano de Investigaciones Científicas, (IVIC), Apartado 1827 Caracas, Venezuela

Received April 7, 1976

Several electron attracting groups have been substituted on the nitrogen atom to decrease the electron density of the pyrrole ring in order to make it more suitable for photoaddition reactions. Once it was found that *N*-benzoylpyrrole is the only compound of the series studied, capable of undergoing oxetane formation, other carbonyl compounds in addition to benzophenone were tested as possible addends to the ring. Successful additions were observed when 3- and 4-benzoylpyridine were used.

J. Heterocyclic Chem., 13, 1037 (1976).

In contrast to furan and its methyl derivatives (1) thiophene and pyrrole have been considered inert to oxetane formation (2).

This lack of reactivity may be due either to the aromatic character of these substances or to the fact that they may be good quenchers of the excited carbonyl compounds.

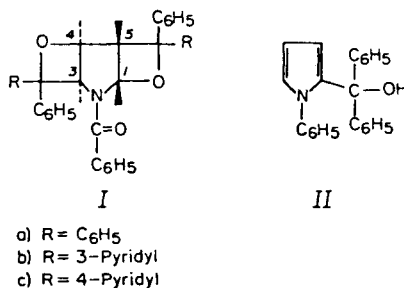
As previously reported the photoaddition of benzophenone to pyrrole to yield an oxetane was possible only when an electron attracting group such as benzoyl was bonded to the nitrogen atom (3).

In order to investigate the scope of this cycloaddition reaction two types of experiments were performed. One type consisted of carrying out irradiations of benzophenone in the presence of *N*-substituted pyrroles where the substituents were electron attracting groups such as benzyl-, carbomethoxy-, benzenesulfonyl-, acetyl-, phenyl-, and benzoyl-. Out of all these substituents only the benzoyl acts effectively to make the pyrrole double bonds suitable for the cycloaddition reaction. In consequence 1-benzoylpyrrole yields a double oxetane Ia; 1-phenylpyrrole yields substitution product II (3) and the other *N*-substituted pyrroles give only polymeric materials. Pyrroles with an electron donating substituent or no substituent at all on the nitrogen atom such as 2,5-dimethyl-, 1-methylpyrrole and pyrrole itself yield only tarry materials.

The other type of reaction consisted in testing the reactivity of 1-benzoylpyrrole towards other excited ketones different from benzophenone, such as, 2-benzoylthiophene, 2-, 3-, and 4-benzoylpyridine, 4-chloro and 4-

methylbenzophenone. Of all the carbonyl compounds in this series only 3- and 4-benzoylpyridine react under photolysis conditions to yield oxetanes Ib and Ic, respectively.

The photoproducts isolated were identified by their nmr and mass spectral data.



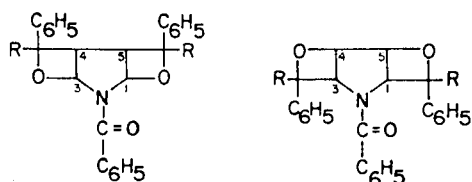
The nmr spectrum of Ia exhibits besides the resonances corresponding to the aromatic protons four doublets at δ 5.80, 5.55, 4.90 and 4.55 ppm respectively ($J_{1,5} = J_{3,4} = 5$ Hz). This information complemented with the mass spectral data agrees with the proposed structure. When a model of the molecule is built, it may be seen that the dihedral angle between hydrogen atoms at carbons 4 and 5 is close to 90° and therefore $J_{4,5} = 0$. Hence, the stereochemistry of Ia is presumably *anti* as shown. If the stereochemistry were *syn*, each ring proton would be coupled with at least two other protons. The nmr spectrum of Ia is very similar to that reported for the corresponding furan derivative (4).

Table I
Nmr Data on the Oxetanes

Oxetane	Protons	Chemical shift (ppm)	Integral and multiplicity	Coupling constants (Hz)
Ia	Aromatic	7.40	25 m	
	C-1	5.80	1 d	$J_{1,5} = 5.0$
	C-3	5.55	1 d	$J_{3,4} = 5.0$
	C-4	4.90	1 d	$J_{3,4} = 5.0$
	C-5	4.55	1 d	
Ib	Aromatic	7.20-8.60	46 m	
	C-1	5.97	2 d (broad)	$J_{1,5} = 5.2$
	C-3	5.52	2 2d	$J_{3,4} = 5.2$
	C-4	4.95	2 2d	
	C-5	4.62	2 2d (overlapping)	
Ic	Aromatic	7.20-8.60	46 m	
	C-1	5.80	2 2d	$J_{1,5} = 5.2$
	C-3	5.47	2 2d	$J_{3,4} = 5.2$
	C-4	4.93	2 d (broad)	
	C-5	4.48	2 2d (overlapping)	

d, doublet; m, multiplet.

By inspection of the nmr spectrum assigned to Ia structures IIIa and IIIb are excluded as possible alternatives for product Ia. If the product were either IIIa or IIIb the nmr spectrum most likely would exhibit only two resonances, in addition to those of the aromatic protons, one corresponding to protons 4 and 5 and the other to protons 1 and 3 since the molecules depicted are symmetrical. The furan analog of Ia can be found in the literature (4) and its nmr spectrum illustrates the appearance of the spectrum for a compound such as IIIa.

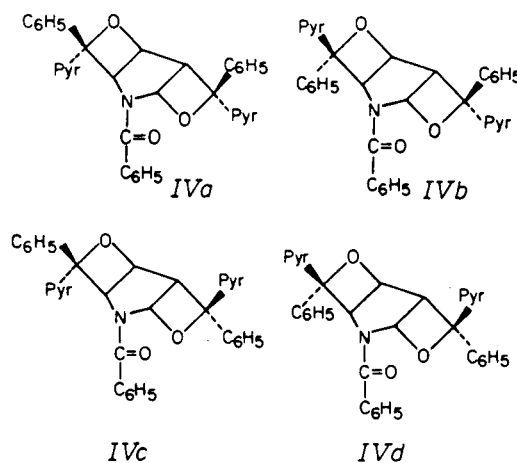


IIIa

IIIb

The nmr spectra of the products derived from 3- and 4-benzoylpyridine disclosed addition of two molecules of carbonyl compound, one to each double bond in the heterocyclic ring. They show that the product is analogous to that obtained from benzophenone. Furthermore, the nmr spectra show two doublets nearly superimposed for each non-aromatic proton. As in the case of the oxetanes obtained from 2,5-dimethylthiophene and from unsymmetrical carbonyl compounds (5) such as the benzoylpyridines, it may be inferred that each photoproduct con-

SCHEME I



IVc

IVd

sists of a mixture of diastereoisomeric oxetanes.

The four possible isomers for each compound may be illustrated by the structures IVa-IVd (Scheme I).

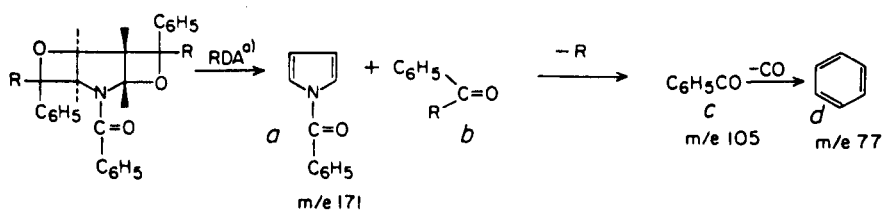
Considering, for instance, the proton at C-3, it can easily be visualized that in two of the possible four isomers this proton may be under the anisotropic influence of a phenyl group and under the anisotropic influence of the pyridyl group in the other two. The same thing may be said for each one of the remaining three non-aromatic protons in the molecule. Following the same reasoning used for the derivatives of 2,5-dimethylthiophene (5) each

Table II
Mass Spectral Data and Physical Constants of the Oxetanes

Oxetane	Yield %	Melting Point °C	M ⁺	Fragments m/e %				R
				a	b	c	d	
Ia	12	222-223	535 1.7	171 17	182 50	105 100	77 100	
Ib	20	180-183	---	171 33	183 19	105 100	77 68	78 16
Ic	30	200-205	---	171 14	183 26	105 100	77 65	78 12.5

a-d as well as R refer to Scheme II.

SCHEME II



a) RDA = Retro Diels Alder

proton should give rise to two doublets as it is observed in the spectra.

The mass spectra of these compounds are characterized by a very small peak or no peak at all for the molecular ion, even at very low bombardment potentials. The main fragmentation pattern involves a double Retro-Diels Alder type process which originates the starting materials, ketone and *N*-substituted heterocyclic. The same type of decomposition was observed for this kind of compounds in Differential Scanning Calorimetry experiments (6). Scheme II shows the main fragmentation pattern for the oxetanes.

The fact that irradiations of carbonyl compounds in the presence of 1-benzoylpyrrole yielded double oxetanes suggested the idea that perhaps decreasing the amount of carbonyl compound in such a way that the ratio of carbonyl compound to heterocyclic be 1:1 in the photolysis reaction would make possible the isolation of pure 1:1 adduct. However, when experiments were carried out using this ratio no product at all was isolated. Since there is no apparent reason for not isolating the 1:1 adduct along with the 2:1 adducts (Ia-Ic) further work will be carried out in order to isolate and characterize such compounds.

EXPERIMENTAL

All the nmr spectra were measured at approximately 30° with a Varian T-60 and an H-60 spectrometers; tetramethylsilane was used as an internal standard. The mass spectra were determined with a Hitachi-Perkin Elmer RMU-6H mass spectrometer. The elemental analyses were performed by Franz Pascher Mikroanalytisches Laboratorium, Bonn, Germany. Benzophenone was used as received from Eastman Kodak. 1-Methyl, 2,5-dimethyl, 1-phenylpyrrole and pyrrole itself were purchased from Aldrich; 1-phenylpyrrole was used as received from Aldrich; the other compounds were distilled before use. 2-Benzoylthiophene, 2-, 3-, and 4-benzoylpyridine, 4-chloro and 4-methylbenzophenone (Aldrich) were purified by crystallization. The *N*-substituted pyrroles, 1-benzene-sulfonyl (7), 1-benzyl (8), 1-carbomethoxy (9), 1-benzoyl (10) and 1-acetylpyrrole (11) were prepared according to different methods in the literature by the general procedure of reacting pyrrole potassium (12) with the corresponding acid chloride in a suitable solvent.

A typical experiment will suffice to illustrate the general procedure for the photolysis reactions.

Photolysis of Benzophenone in the Presence of 1-Benzoylpyrrole.

A solution of 1 g. (0.0058 mole) of 1-benzoylpyrrole and 3 g. (0.0164 mole) of benzophenone in 100 ml. of benzene was placed in a reaction vessel. A quartz immersion well fitted into the reaction vessel and a pyrex filter and a Hanovia 450 watt lamp were placed inside the immersion well. The solution was then

irradiated at about 40° while nitrogen gas was passed through the irradiation vessel. After 24 hours exposure to uv light the irradiation was stopped and the solvent distilled under vacuum. The residue was chromatographed in an alumina column (25 g. of alumina per gram of residue). The useful fraction consisted of an oil which under treatment with acetone solidified, m.p. 222-223, 12% yield on the basis of 1-benzoylpyrrole consumed.

Anal. Calcd. for $C_{37}H_{29}NO_3$: C, 83.00; H, 5.48; N, 2.62. Found: C, 82.66; H, 5.51; N, 2.94.

Other Photolysis Reactions.

These reactions were carried out as illustrated above for benzophenone and 1-benzoylpyrrole. The total yields calculated on the basis of 1-benzoylpyrrole consumed are given in Table II. The infrared spectra exhibited bands at 3,060, 3,030 (aromatic str.); 1,650 (conjugated -CO-); 980 cm^{-1} (trimethylene oxide ring).

Elemental analyses for Ib and Ic: Calcd. for $C_{35}H_{27}N_3O_3$: C, 78.20; H, 5.03; N, 7.82. (Ib) Found: C, 77.84; H, 5.20; N, 7.21. (Ic) Found: C, 77.90; H, 5.08; N, 7.10.

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