

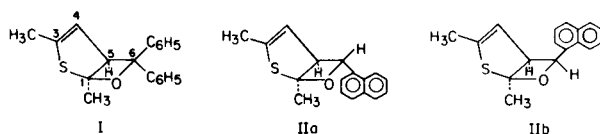
## Synthesis of Oxetanes by Photoaddition of Carbonyl Compounds to 2,5-Dimethylthiophene

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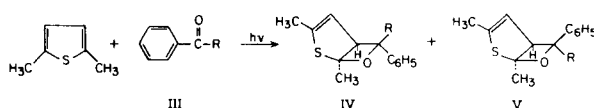
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As previously reported the photoaddition of benzophenone to 2,5-dimethylthiophene to yield an oxetane (I) was carried out successfully in this laboratory (1). In contrast to thiophene and other methyl-substituted thiophenes, 2,5-dimethylthiophene has been the only member of the series to undergo this type of reaction.



In order to investigate the scope of this cycloaddition reaction, carbonyl compounds such as 1- and 2-naphthaldehyde, benzaldehyde, 2-,3- and 4-benzoylpyridine, 1-benzoylpyrrole, acetophenone and 2-benzoylthiophene, respectively, were irradiated in 2,5-dimethylthiophene. Out of these carbonyl compounds only 1-naphthaldehyde, 2-,3- and 4-benzoylpyridine and 2-benzoylthiophene react with the substrate to yield oxetanes (II, IV and V).



a) R = 2-Pyridyl  
b) R = 3-Pyridyl

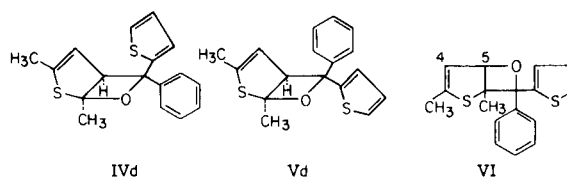
c) R = 4-Pyridyl  
d) R = 2-Thienyl

The nmr, mass spectra and physical data of the products are presented in Tables I, II and III.

It is interesting to note that all these asymmetric carbonyl compounds ( $R \neq$  phenyl) yield oxetanes which are present as a mixture of two geometrical isomers IV and V; the presence of these isomers may be inferred from the nmr spectra of the compounds.

The best example of this type of mixture can be observed in the oxetanes obtained by cycloaddition of 2-benzoylthiophene to 2,5-dimethylthiophene. The nmr spectrum of the mixture exhibits two sets of identical signals for each non aromatic proton. This fact suggests the presence of two compounds of very similar structure.

Since the two sets of identical signals for each proton appear next to each other it is not reasonable to propose a structure such as VI for one of the isomers because the chemical shift for the proton at C-5 in VI would be different from that observed for protons in that position



not only in these compounds, but in other reported earlier (2). After reconsidering the chemical shifts reported for compound I (1,6) and comparing the values given with those reported for similar compounds (2) it appears more reasonable to assign  $\delta = 4.96$  and  $\delta = 4.50$  ppm to protons at C-4 and C-5, respectively.

The nmr spectrum of the mixture of compounds IVd and Vd exhibits two sextets at 4.80 and 4.90 ppm corresponding to protons at C-4 and two more sextets at 4.50 and 4.40 ppm (partially overlapping) which correspond to protons at C-5 in IVd and Vd, respectively.

Since in compound I the protons at C-4 and C-5 are only influenced by phenyl groups, one may speculate that

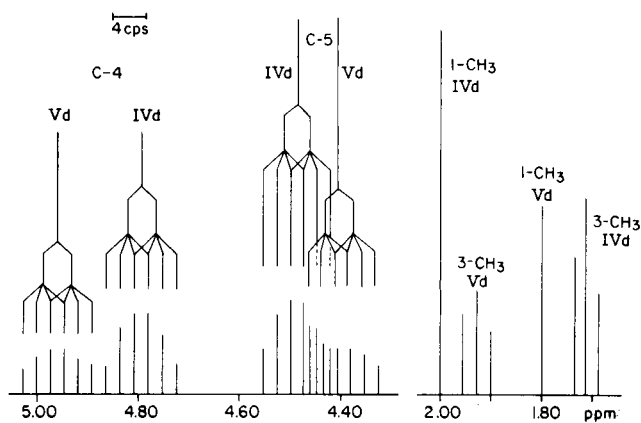


Fig. 1. Nmr Spectrum of IVd and Vd

TABLE I

## NMR DATA ON THE OXETANES

Oxetane	Protons	Chemical shift (ppm)	Integral and multiplicity	Coupling constants (Hz)
IIa	1-CH <sub>3</sub>	1.95	3 s	$J_{5,6} = 3.5$
IIb	3-CH <sub>3</sub>	2.10	3 m	
	C-4	5.60	1 m	$J_{3-CH_3,4} = 1.5$
	C-5	3.65	1 m	$J_{3-CH_3,5} = 1.5$
	C-6	6.20	1 d	
IVa	1-CH <sub>3</sub>	1.82 and 1.72	3 s; 3 s	$J_{3-CH_3,4} = J_{3-CH_3,5} = 1.5$
Va	3-CH <sub>3</sub>	1.72 and 1.67	3 t; 3 t	$J_{4,5} = 2.8$
	C-4 and C-5	4.40; 5.00; 4.80	1 sextet; 1 sextet; 2 m	
IVb	1- and 3-CH <sub>3</sub>	1.80	6 s; 6 t	$J_{3-CH_3,4} = 1.4$
Vb	C-4	4.83	2 m	$J_{3-CH_3,5} = 1.4$
	C-5	4.46	2 m	
IVc	1- and 3-CH <sub>3</sub>	1.80	6 s; 6 t	$J_{3-CH_3,4} = J_{3-CH_3,5} = 1.6$
Vc	C-4	4.83	2 sextet, sextet	$J_{4,5} = 3.2$
	C-5	4.36	2 sextet, sextet	
IVd	1-CH <sub>3</sub>	2.00	3 s	$J_{3-CH_3,4} = J_{3-CH_3,5} = 1.6$
	3-CH <sub>3</sub>	1.75	3 t	$J_{4,5} = 3.2$
	C-4	4.80	1 sextet	
	C-5	4.50	1 sextet	
	Thienyl	6.70 - 7.00	3 m	
Vd	1-CH <sub>3</sub>	1.80	3 s	$J_{3-CH_3,4} = J_{3-CH_3,5} = 1.6$
	3-CH <sub>3</sub>	1.90	3 t	
	C-4	4.90	1 sextet	$J_{4,5} = 3.2$
	C-5	4.40	1 sextet	
	Thienyl	6.70 - 7.00	3 m	

The chemical shift for the aromatic protons in IIa and IIb is found at 7.8 ppm; in the other compounds it is found at 7.3 ppm. s, singlet; d, doublet; t, triplet; m, multiplet.

perhaps the signal at 4.90 ppm corresponds to the proton at C-4 in Vd and that the signal at 4.50 ppm is produced by the proton at C-5 in IVd. These are the protons under the influence of the phenyl group in each isomer as may be visualized by the use of molecular models. Therefore, if this assignment were true, the signals at 4.80 and 4.40 ppm would correspond respectively to protons at C-4 in IVd and C-5 in Vd.

The methyl groups appear also as two sets of signals; each set consists of a triplet and a singlet (1.75 t; 1.80

s; 1.90 t; 2.00 ppm s).

Since the integrals of the resonances at 4.90 and 4.40 ppm which were assigned to protons at C-4 and C-5 in Vd, are in a ratio of 36/64 with respect to those at 4.80 and 4.50 ppm which were assigned to the same protons in IVd, it may be assumed that compound IVd is formed in greater yield than compound Vd. By the same token, since the same relationship is observed in the resonances corresponding to the methyl groups, one can presumably

TABLE II  
 MASS SPECTRAL DATA ON THE OXETANES m/e./%

OXETANE	M <sup>+</sup>	a	b	c	d	e	f	g	h	i	j	k	R	R'
IIa, IIb	268	112	156	111	97	53	59	225	-	155	193	177	-	127
	2	100	67	67	39	5	13	-	-	43	-	-	-	66
IVa, Va	295	112	183	111	97	53	59	252	106	105	220	204	77	78
	-	100	20	96	55	7	15	1	6	58	1	-	69	21
IVb, Vb	295	112	183	111	97	53	59	252	106	105	220	204	77	78
	1	100	20	41	20	2	6	1	5	23	1	2	21	8
IVc, Vc	295	112	183	111	97	53	59	252	106	105	220	204	77	78
	1,5	100	6	29	10	2	4	1,5	2	12	1	2	13	3
IVd, Vd	300	112	188	111	97	53	59	257	111	105	225	209	77	83
	22	100	12	38	27	6	11	18	10	8	27	3	14	2

a - k as well as R and R' refer to Scheme I

assign the singlet at 2.00 ppm and the triplet at 1.75 ppm to 1-CH<sub>3</sub> and 3-CH<sub>3</sub>, respectively in IVd, which are the signals whose integrals represent the larger value (64%) and therefore belong to the methyl groups of the isomer formed in larger quantity. The nmr spectrum of the mixture of compounds IVd and Vd is illustrated in Figure 1.

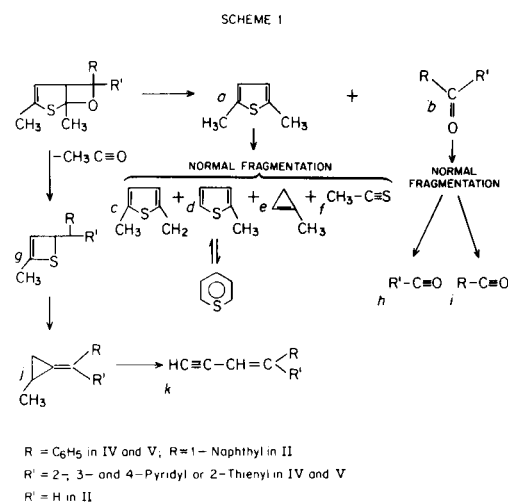
In the oxetanes derived from the 2-benzoylpyridine, protons at C-4 and C-5 appear as two sextets, one at 4.40 ppm and another at 5.00 ppm. Between these two signals at 4.80 ppm there is a multiplet which corresponds to two overlapping sextets; the ratio of the integral of this multiplet to each one of the other two sextets is 53.5/46.5. The methyl groups appear as one triplet at 1.67 ppm and as a singlet at 1.82 ppm and between these two a signal at 1.72 ppm which contains a singlet and a triplet. The ratio of the integral of this signal to each of the other two methyl resonances is the same as the ratio for the former signals corresponding to protons at C-4 and C-5. Comparing the chemical shifts observed in this spectrum with those in that for the oxetane derived from benzophenone, compound I, it may be speculated that the ratio of compound Va to IVa formed is 53.5/46.5. The presence of two isomers in the spectrum of the oxetane derived from 1-naphthaldehyde may be inferred from the doublet at 6.20 ppm, corresponding to proton at C-6 whose doublet appears as two broad peaks. The presence of two compounds in the product derived from 1-naphthaldehyde is less obvious than in the previous cases.

The 3- and 4-benzoylpyridines yield mixtures of oxetanes where protons at C-4 and C-5 appear as two sextets overlapping almost completely and the methyl groups appear as one signal where a triplet and a singlet are discernible.

The mass spectra of all these compounds exhibit fragmentation patterns characteristic of the 2,5-dimethylthiophene (3,4) moiety and of the corresponding carbonyl compound (3). The initial step in the fragmentation process presumably is of a retro-Diels-Alder type in which the original 2,5-dimethylthiophene and the corresponding carbonyl compound are formed. The mass spectra of oxetanes of the type reported here will be discussed elsewhere (5).

Scheme I is given as complementary to Table II and is based on a fragmentation mechanism found for different oxetanes derived from five-membered heterocyclics (5).

The carbonyl compounds tested for oxetane formation in this investigation do not yield adducts with thiophene and 2-methylthiophene. The stereochemistry of the junction between the five- and four-membered rings (at carbons 1 and 5) in this type of compound is discussed elsewhere (6).



## EXPERIMENTAL

All nmr spectra were measured at approximately 30° with a Varian XR-100 and a T-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. 2-,3- and 4-Benzoylpyridine and 2-benzoylthiophene (Aldrich) were purified by crystallization; 1-naphthaldehyde (Aldrich) was purified by distillation under reduced pressure. 2,5-Dimethylthiophene was distilled before use and alternatively also used as received from Aldrich; the results were equally good.

The general procedure for the photolysis reactions was to dissolve 1 g. of the carbonyl compound under investigation in 75 ml. of 2,5-dimethylthiophene. The reaction mixture was irradiated with a Hanovia 450 w mercury arc in a quartz apparatus with a pyrex filter sleeve, at -10°. Nitrogen was bubbled through the solution before and during irradiation. After 8 hours exposure to uv light, the irradiation was stopped and the solvent distilled under vacuum. The residue in most cases crystallized by itself; in case it did not solidify, treatment with methanol induced crystallization. The infrared spectra of the oxetanes exhibited the characteristic methyl stretching bands at 2959 cm<sup>-1</sup> and the four-membered oxygenated ring at 980 and 995 cm<sup>-1</sup>. The separation of isomers has not been possible by chromatographic methods.

All these mixtures of isomeric oxetanes were chromatographed on Merck TLC plastic sheets silica gel F<sub>254</sub> using benzene as well as ether as eluents; always one spot was observed or otherwise several spots corresponding to decomposition products. The product derived from 1-naphthaldehyde was also chromatographed on a silica gel column starting with mixtures of benzene-petroleum ether and continuing with pure benzene as eluent; chromatography was stopped when the product decomposed on the column. Decomposition was detected because large quantities of 1-naphthaldehyde were collected. Attempts were made to separate the oxetanes derived from the benzoylpyridines by means of reverse phase chromatography using an HPLC-Dupont 840 instrument equipped with an ETH 1m column with methanol 65% as mobile phase and 800 psi, no separation was observed. The

TABLE III

## PHYSICAL CONSTANTS FOR THE OXETANES

Oxetane	M.p.	Molecular weight	Yield %	Empirical formula	Analysis			
					Calcd. Found	C	H	S
IIa and IIb	115-118	268	50	C <sub>17</sub> H <sub>16</sub> O S	-	-	-	-
IVa and Va	107-110	295	62	C <sub>18</sub> H <sub>17</sub> N O S	73.22 72.78	5.76 5.87	10.84 10.96	4.74 4.83
IVb and Vb	136	295	58	C <sub>18</sub> H <sub>17</sub> N O S	73.22 72.86	5.76 5.75	10.84 10.83	4.74 5.02
IVc and Vc	Sublimes	295	60	C <sub>18</sub> H <sub>17</sub> N O S	73.22 73.15	5.76 5.81	10.84 10.77	4.74 4.71
IVd and Vd	116	300	50	C <sub>17</sub> H <sub>16</sub> O S <sub>2</sub>	-	-	-	-

The molecular weights were determined from the mass spectra. The yields were calculated on the basis of carbonyl compound consumed. Compounds IIa, IIb, IVd and Vd slowly decompose outside the ice box; therefore no reliable elemental analysis could be performed on them.

oxetanes from 2-benzoylthiophene are so unstable outside the ice box that no attempt was made to chromatograph them.

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