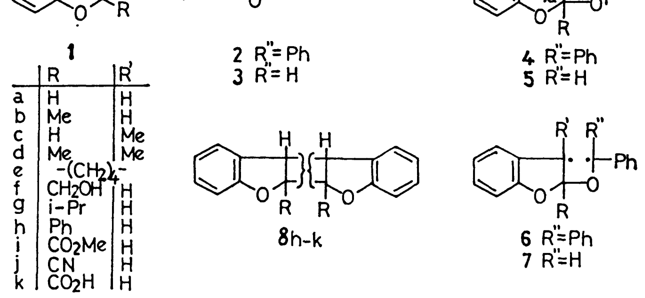
The Photochemical Reaction of Benzofuran Derivatives with Benzophenone or Benzaldehyde

Yoshiyuki Kawase, Seiji Yamaguchi, Hirokazu Ochiai, and Hisanori Horita
Department of Chemistry, Faculty of Literature and Science, Toyama University, Gofuku, Toyama 930

(Received February 15, 1974)

The photochemical reaction of 2-methyl-, 2,3-dimethyl-, 2,3-butano-, and 2-hydroxymethyl-benzofuran with benzophenone gave the corresponding oxetanes in yields higher than, or comparable to, those in the case of unsubstituted benzofuran, but in lower yields than in the cases of 3-methyl- and 2-isopropyl-benzofuran. The oxetanes were also produced by the reaction of 2-methyl-, 2,3-dimethyl-, and 2,3-butano-benzofuran with benzaldehyde, but these yields were not so high because of their instability. The reaction of 2-methoxycarbonyl- and 2-cyano-benzofuran with benzophenone or benzaldehyde gave dimers of the benzofurans, as in the case of 2-phenylbenzofuran.

It has been reported that the photochemical reaction of furan derivatives with carbonyl compounds furnished the oxetanes;[1] also, a similar reaction of benzofuran with benzophenone or benzaldehyde furnished the oxetane, while benzofuran with acetone or acetophenone as well as 2-phenylbenzofuran with benzophenone or benzaldehyde furnished the cyclo-dimer of the benzofuran.[2] Now in the present experiments, the reaction of 2-, 3-, and 2,3-substituted benzofurans (**1**) with benzophenone (**2**) or benzaldehyde (**3**) was studied in order to investigate the effect of the substituents.



1

2 R''=Ph
3 R''=H

4 R''=Ph
5 R''=H

8h-k

6 R''=Ph
7 R''=H

	R	R'
a	H	H
b	Me	H
c	H	Me
d	Me	Me
e	-(CH$_2$)$_4$-	
f	CH$_2$OH	H
g	i-Pr	H
h	Ph	H
i	CO$_2$Me	H
j	CN	H
k	CO$_2$H	H

A benzene solution of a benzofuran derivative (**1a**—**j**) and benzophenone (**2**) or benzaldehyde (**3**) was irradiated for several hours by means of a 100 W high-pressure mercury lamp in a nitrogen atmosphere, the solvent was removed *in vacuo*, and the residual product was crystallized. In several cases, the reaction rate was checked by NMR spectroscopy. It was found that the reaction mixture contained only one kind of product and the starting materials, and that the yield of the product reached a maximum at about 20 hr irradiation in the case of **1a**, **b**, and **d** with **2**, while it reached a maximum at about 8 hr irradiation in the case of **1a**, **b**, and **d** with **3**. Therefore, the reaction was stopped at those times. The reaction of **1b**, **d**, **e**, and **f** with **2** furnished the corresponding oxetanes (**4b**, **d**, **e**, and **f**) in yields higher than, or comparable to, those in the case of benzofuran[2] (**1a**), but **1c** and **1g** furnished the oxetanes (**4c** and **4g**) in low yields only. In the case of the reaction of **1a**—**e** with **3**, a fairly large amount (about a 60% yield) of the oxetane (**5a**—**e**) was detected in the reaction mixture. However, not much of the pure product was isolated because of the instability of the oxetane; particularly the pure **5c** could not be isolated.

The structures of the oxetanes (**4** and **5**) were determined by elemental analyses and by spectroscopy (IR, NMR, and Mass), particularly by comparing their NMR data with those[2] of **4a** and **5a**. That is, the structures of **4b**, **4f**, **4g**, and **5b** were determined by means of the fact that the chemical shifts of 2a-H of **4b**, **4f**, **4g** (δ=4.56, 5.02, 4.82) and of **5b** (δ=3.83) were comparable with those of **4a** (δ=4.97) and **5a** (δ=4.12) respectively. Also, the structure of **4c** was determined by means of the chemical shift of 7a-H (δ=6.21) being comparable with that of **4a** (δ=6.50). Upon the basis of these data, the structure of **4d** was determined by means of the fact that the chemical shifts of 2a- and 7a-methyl hydrogen (δ=1.65 and 1.64) were comparable with those of **4c** and **4b** (δ=1.40 and 1.61) respectively, while the structure of **5d** was determined by means of the fact that the shift of 7a-methyl hydrogen (δ=1.64) was comparable with that of **5b** (δ=1.75). Further, **4e** and **5e** were considered to have the structures shown in the chart by analogy to the cases of **4d** and **5d**. The configuration of the oxetanes (**5**) at the C$_2$-position has not yet been determined, but it seemed that the C$_2$-phenyl groups of **5a** and **5b** might be *cis* to the 2a-H, by analogy to the case of the oxetane produced from furan and benzaldehyde.[1g]

In the present reaction, the intermediate biradical, **6** or **7**, may be formed by the electrophilic attack of the oxygen radical of the excited triplet state of the carbonyl group, and the oxetane may be formed by the intra-molecular coupling of the biradical, as in the case of the reaction of furan derivatives with carbonyl compounds.[1] The alkyl groups (R and R') on the furan ring may facilitate the attack of the oxygen radical and increase the stability of the intermediate biradical; they may thus favor the formation of the oxetane. Indeed, in the reaction of the benzofuran derivative with benzophenone, the yields of the oxetane formation in the case of **4b**, **d**, and **e** are much higher than those of unsubstituted benzofuran. However, it seems necessary to consider the steric hindrance in order to explain the low yields of **4g** and **4c** and the yield of **4d** being lower than that of **4b**. In the reaction of the benzofuran derivative with benzaldehyde, the yield of the oxetane is not very high, and the oxetane is unstable on standing. It seems that these facts are

TABLE 1. THE PHOTO-CHEMICAL REACTION

Starting compounds	Reaction time (hr)	Product (yield, %)	Mp °C (solvent[i])	NMR: δ (ppm) of H of R	R′	R″	solv.	Mass M$^+$ (m/e)
1a+**2**	20	**4a**(27[ii])	133—134[ii] (Me)	6.50[ii]	4.97[ii]		$CDCl_3$	300
1b+**2**	20	**4b**(79)	130—132(Pe)	1.61	4.56		$CDCl_3$	314
1c+**2**	51	**4c**(2)	157—158.5 (Cy)	6.21	1.40		CCl_4	314
1d+**2**	20	**4d**(62)	193—194 (Cy)	1.65	1.43		$CDCl_3$	328
1e+**2**	20	**4e**(44)	174.5—176 (Cy)	2.75—0.90			$CDCl_3$	354
1f+**2**	20	**4f**(27)	164—165 (Ac)	3.83, 1.85	5.02		$CDCl_3$	330
1g+**2**	20	**4g**(6)	137.5—138.5 (Cy)	2.14, 1.03, 0.94	4.83		$CDCl_3$	342
1a+**3**	8	**5a**(30[iii])	96—97[iii] (Me)	6.60[iii]	4.12[iii]	5.45[iii]	$CDCl_3$	224
					J=3.4[iii]			
1b+**3**	8	**5b**(39)	78—81 (Pe)	1.75	3.83	5.32	CCl_4	238
					J=4.0			
1d+**3**	8	**5d**(42)	92—93 (Cy)	1.64	0.94	5.45	CCl_4	252
1e+**3**	8	**5e**(11)	83—84 (Me)	2.85—0.90		5.72	$CDCl_3$	iv)
1h+**2**	65	**8h**(1.5[v])	265—266[v] (Cl)		4.80[v]		$CDCl_3$	388
1h+**3**	12	**8h**(2[v])	265—266[v] (Cl)		4.80[v]		$CDCl_3$	388
1i+**2**	20	**8i**(2)	258—259 (Ac)	3.55	4.96		CF_3CO_2H	352
1i+**3**	20	**8i**(2)	258—259 (Ac)	3.55	4.96		CF_3CO_2H	352
1j+**2**	15	**8j**(27)	276.5—277.5 (Ac)					286
1j+**3**	15	**8j**(10)	276.5—277.5 (Ac)					286

i) Ac=acetone, Cl=chloroform, Me=methanol, and Pe=petroleum ether. ii) *Cf.* Ref. 2. Lit, mp 132 °C. iii) *Cf.* Ref. 2. Lit, mp 95—96 °C. iv) This was not detectable. v) *Cf.* Ref. 2. Lit, mp 279—280 °C.

due to the formation of the not-very-much-stabilized intermediate biradical, **7**; the stabilizing effect of the R and R′ groups is not great enough to improve the stability of **7**.

The reaction of 2-methoxycarbonyl- and 2-cyanobenzofuran (**1i** and **1j**) with **2** or **3** gave dimers (**8i** and **8j**) of the benzofurans in low yields, much as in the case of 2-phenylbenzofuran[2] (**1h**). The hydrolysis of **8i** as well as **8j** gave the same carboxylic acid, **8k** (**8**(R=CO_2H)). The structures of **8h**—**k** have not yet been established. In the reaction of **1i** and **1j** with **2** or **3**, it seems that the energy level of the excited benzofuran derivative is lowered by conjugation with the substituent, and **1i** and **1j** receive energy from the excited carbonyl compound to react with another molecule of **1i** and **1j**, the carbonyl compound having been used as a sensitizer.

Experimental

The melting points were not corrected; the IR spectra were measured on a Hitachi EPI-S spectrophotometer, the NMR spectra, on a JEOL JNM-C-60H (60 MHz) spectrometer, and the mass spectra, on a JEOL JMS-OIS spectrometer. The data are summarized in the tables.

Materials. The benzofuran[3] (**1a**), 2-methylbenzofuran[4] (**1b**), 3-methylbenzofuran[5] (**1c**), 2,3-dimethylbenzofuran[6] (**1d**), 2,3-butanobenzofuran[7] (**1e**), 2-benzofuranylmethyl alcohol[8] (**1f**), 2-phenylbenzofuran[9] (**1h**), methyl 2-benzofurancarboxylate[8] (**1i**), and 2-benzofurancarbonitrile[10] (**1j**) were prepared by the literature procedures. The 2-isopropylbenzofuran (**1g**) was prepared by the action of diethyl isopropylmalonate on salicylaldehyde, as will be reported later.

The Photochemical Reaction of the Benzofuran Derivative (1) with Benzophenone (2) or Benzaldehyde (3). A benzene solution of **1** and **2** or **3** (each 0.02 mol in 200 ml of benzene) was irradiated by means of a 100 W high-pressure mercury lamp through a Pyrex jacket (Rikosangyo Co.) in a nitrogen atmosphere at 20—25 °C for several hours, as is shown in the table. The solvent was then removed *in vacuo*, and the residual product was crystallized from the solvent shown in the table.

TABLE 2. ELEMENTAL ANALYSES OF THE NEW COMPOUNDS

Compound	Found (%) C	H	N	Formula	Calcd (%) C	H	N
4b	84.25	5.61		$C_{22}H_{18}O_2$	84.05	5.77	
4c	84.26	5.80		$C_{22}H_{18}O_2$	84.05	5.77	
4d	84.40	6.24		$C_{23}H_{20}O_2$	84.12	6.14	
4e	84.71	6.20		$C_{25}H_{22}O_2$	84.71	6.26	
4f	80.19	5.43		$C_{22}H_{18}O_3$	79.98	5.49	
4g	84.28	6.52		$C_{24}H_{22}O_2$	84.17	6.47	
5b	80.86	5.86		$C_{16}H_{14}O_2$	80.64	5.92	
5d	80.65	6.66		$C_{17}H_{16}O_2$	80.92	6.39	
5e	81.72	6.52		$C_{19}H_{18}O_2$	81.98	6.52	
8i	68.26	4.56		$C_{20}H_{16}O_6$	68.18	4.58	
8j	75.70	3.50	9.83	$C_{18}H_{10}O_2N_2$	75.51	3.52	9.79
8k	66.68	3.73		$C_{18}H_{12}O_6$	66.67	3.73	

The Hydrolysis of 8i. A mixture of **8i** (0.2 g), 50% aqueous potassium hydroxide (2 g), and methanol (2 ml) was refluxed for 3 hr. The reaction mixture was then treated as usual, and the product was crystallized from acetone to give 0.1 g (50%) of an acid, **8k**; mp 332 °C (decomp.), ν_{max}^{KBr} cm^{-1}: 3450—2510 (OH), 1712 (CO).

The Hydrolysis of 8j. A mixture of **8j** (0.5 g), 50% aqueous potassium hydroxide (6 g), and ethylene glycohol (5 ml) was heated at 100 °C for 8 hr. The reaction mixture was then diluted with water and acidified. The precipitates thus obtained were crystallized from acetone to give 0.15 g (26%) of **8k**, identical with the other sample.

References

1) a) G. O. Schenck, W. Hartmann, and R. Steinmetz, *Chem. Ber.*, **96**, 498 (1963); b) G. S. Hammond and N. J. Turro, *Science*, **142**, 1541 (1963); c) S. Toki, K. Shima, and H. Sakurai, This Bulletin, **38**, 760 (1965); K. Shima and H. Sakurai, *ibid.*, **39**, 1809 (1966); S. Toki and H. Sakurai, *Tetrahedron Lett.*, **1967**, 4119; d) J. Leitich, *ibid.*, **1967**, 1937; e) C. Rivas and E. Payo, *J. Org. Chem.*, **32**, 2918 (1967); f) M. Ogata, H. Watanabe, and H. Kano, *Tetrahedron Lett.*, **1967**, 533; g) G. R. Evanega and E. B. Whipple, *ibid.*, **1967**, 2163; E. B. Whipple and G. R. Evanega, *Tetrahedron*, **24**, 1299 (1968).

2) C. H. Krauch, W. Metzner, and G. O. Schenck, *Chem. Ber.*, **99**, 1723 (1966).

3) A. W. Burgstahler and L. R. Worden, "Organic Syntheses," Vol. 46, p. 28 (1965).

4) T. Abe and T. Shimizu, *Nippon Kagaku Zasshi*, **91**, 753 (1970).

5) W. R. Boehme, "Organic Syntheses," Coll. Vol. IV, p. 590, (1963).

6) E. Bisagni and R. Royer, *Bull. Soc. Chim. France*, **1962,** 925.

7) F. Ebel, *Helv. Chim. Acta*, **12**, 3 (1929).

8) B. I. Nurunnabi, *Pakistan J. Sci. Ind. Research*, **3**, 108 (1960) (*Chem. Abstr.*, **55**, 25903 (1961)).

9) S. Kawai, T. Nakamura, and N. Sugiyama, *Chem. Ber.*, **72**, 1146 (1939).

10) L. Roné and R. Royer, *Bull. Soc. Chim. France*, **1971,** 4329.