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PHOTOCHEMISTRY OF HETEROCYCLIC COMPOUNDS—II[1]

THE PHOTOCHEMICAL REACTION OF 2,5-DISUBSTITUTED 1,3,4-OXADIAZOLES WITH FURAN

O. TSUGE,* K. OE and M. TASHIRO
Research Institute of Industrial Science, Kyushu University, Hakozaki, Higashi-ku,
Fukuoka 812, Japan

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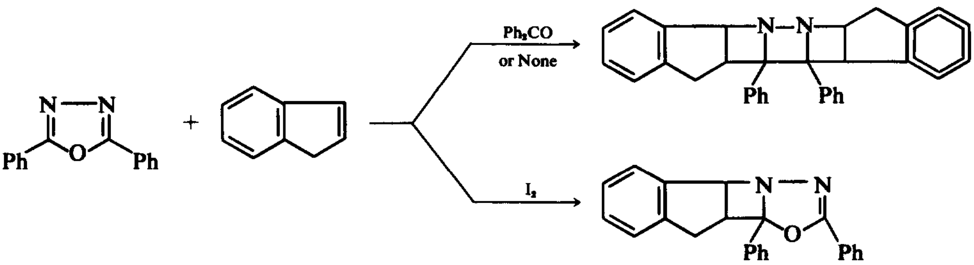
Abstract—The photochemical reaction of 2,5-disubstituted 1,3,4-oxadiazoles with furan has been studied. With or without benzophenone as a sensitizer, irradiation of 2,5-diphenyl-1,3,4-oxadiazole with furan in benzene solution gives the 1:1 cycloadduct, tetrahydrofuro[2·3-b]azetidino[2·1-b]-1,3,4-oxadiazole. However in the presence of iodine 3-acylfurans and their acylhydrazones are formed. A reaction pathway of this novel photo-induced acylation has been suggested.

The photochemical reaction of 2,5-diphenyl-1,3,4-oxadiazole with indene with or without benzophenone as a sensitizer, affords a novel diazetidine derivative,[1] while in the presence of iodine the 1:1 cyclo adduct, indeno[2·3-c]azetidino[2·1-b]-1,3,4-oxadiazole, is formed.[1] We now wish to report the photochemical reaction of 2,5-disubstituted 1,3,4-oxadiazoles with furan which leads to the formation of novel products.



RESULTS AND DISCUSSION

With and without benzophenone as sensitizer. When a solution of 2,5-diphenyl-1,3,4-oxadiazole (**1a**) and excess furan was irradiated, an 1:1 adduct (**2**) m.p. 179–181°, was obtained in 18% yield. With benzophenone (10 mole % to **1a**), the yield of **2** was 26%; no products arising from the photoreaction of furan with benzophenone were formed[2] and benzophenone was recovered quantitatively.

The 1,2-1,2, 1,2-1,4 and 1,4-1,2 cycloadducts of **1a** to furan are possible for the structure of **2**, because both **1a** and furan are 1,3-diene-like structures. However, on the basis of the IR spectrum which shows a band ascribable to $\nu_{C=N}$ and of the NMR spectrum (Fig 1), both 1,2-1,4 and 1,4-1,2 cycloadducts can be excluded for the structure of **2**. Thus, the 1,2-1,2 cycloadducts **2a** and **2b**, are conceivable for the structure of **2** (Scheme 1).

Hydrogenation of **2** over the Adams' catalyst led to the formation of dihydro compound **3**, whose IR spectrum displayed the band ascribable to $\nu_{C=N}$; thus structure **3a** or **3b** can be assigned to **3** (Scheme 1).

Gagnaire and Payo-Subiza[3] established the structure of the 1:1 photoadduct of furan to benzophenone to be the oxethane A but not B on the basis of NMR spectral data of the adduct and its dihydro compound. The proton signals and coupling constants assigned for A are as follows.

The NMR spectrum of **2** is illustrated in Fig 1. Among four non-aromatic protons, H_c in **2a** adjacent to both an N and an O atom and H_d in **2b** would be expected to appear at the low field respectively. Based on Gagnaire's assignment for A, a multiplet would be expected for H_d in **2**. As illustrated in Fig 1, however, the signal at τ 3·07 appears as a doublet; this strongly suggests that it be assigned to H_c in **2a** and not to H_d in **2b**. Furthermore, the doublet at τ 3·07 and the double doublet at τ 3·35 become a singlet and a doublet respec-

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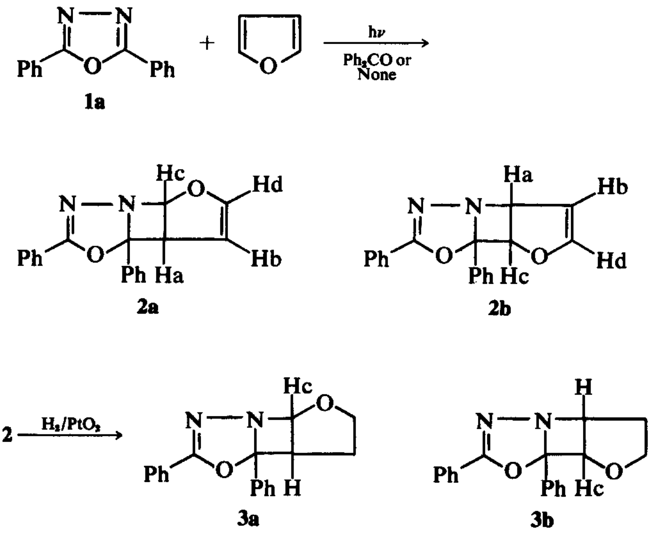
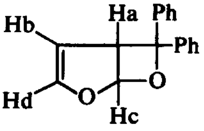
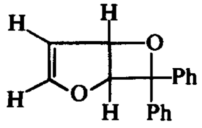
*To whom correspondence should be directed.



SCHEME 1



A



B

τ	Hz
$H_a = 5{\cdot}70$	$J_{ab} = 3{\cdot}1$
$H_b = 5{\cdot}21$	$J_{ac} = 4{\cdot}5$
$H_c = 3{\cdot}80$	$J_{ad} = 1{\cdot}3$
$H_d = 3{\cdot}69$	$J_{bc} = 0$
	$J_{bd} = 2{\cdot}9$
	$J_{cd} = 0{\cdot}8$

tively, when the multiplet at τ 5·80 is irradiated (assignable to the proton H_a in **2**).* In addition, H_c in the dihydro derivative **3** appeared at τ 3·13 as an unsymmetrical singlet.

On the basis of these observations, it was deduced that photoadduct **2** is 3a,3b,6a,6b-tetrahydro-2,6b-diphenylfuro[2·3-b]-azetidino[2·1-b]-1,3,4-oxadiazole (**2a**) and thus, the dihydro compound **3** is hexahydrofuro[2·3-b]azetidino[2·1-b]-1,3,4-oxadiazole (**3a**). The coupling constants between the protons at positions 3b and 6a suggest that these hydrogens in **2a** and **3a** are *trans*.

Irradiation in the presence of benzophenone increased the yield of **2a**, while **2a** was not formed in the presence of piperylene as a triplet quencher, indicating that the photoaddition reaction proceeds *via* an excited triplet state.

In the presence of iodine. A similar irradiation of **1a** and furan in the presence of iodine (20 mole%

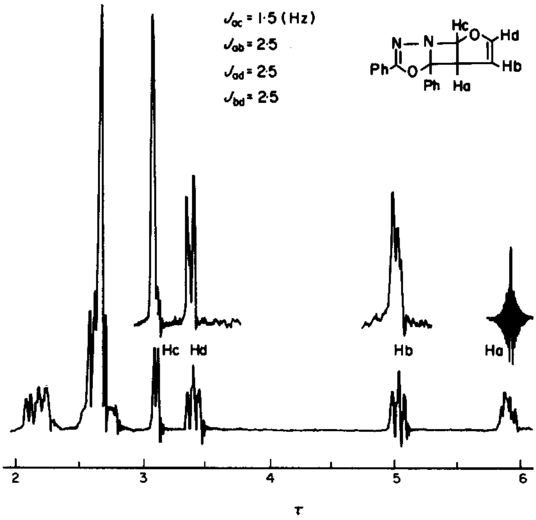


Fig 1. NMR spectrum of **2** in $CDCl_3$.

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*As expected, Hb changed to a doublet upon irradiation at τ 5·80, the appearance of an unshapely peak being probably due to the close proximity of the irradiation position.

to **1a**) afforded 16·5% of a product **4a** as yellow viscous oil. Photolysis with cooling gave products **4a** and **5a**, m.p. 125–126°, in 10 and 3% yield respectively. In both runs, **1a** was recovered in 50% yield, while in neither cases was any **2a** formed. Recovery of **1a** in large amounts is due to the lowering of light transmission as a muddy solution formed during irradiation.

The IR spectrum of **4a** ($C_{11}H_8O_2$) showed the band ascribable to $\nu_{C=O}$ at 1660 cm^{-1}, while dihydro compound **6**, m.p. 65–65·5°, obtained quantitatively from the reduction of **4a** with $NaBH_4$, exhibited a band assignable to ν_{OH} at 3200 cm^{-1}. On the basis of the IR and NMR spectra (Fig 2), it was assumed that **4a** is either 2- or 3-benzoylfuran and **6** the corresponding carbinol. Although the spectral data did not permit a clear assignment, we found that **4a** is different from authentic 2-benzoylfuran;[4] the IR spectra of **4a** and 2-benzoylfuran were very similar. This leaves little doubt that **4a** is 3-benzoylfuran and **6** the corresponding carbinol. The mass spectra of **4a** and **6** further support the proposed structures.

However, product **5a** which corresponds to a 1:1 adduct showed the characteristic bands ascribable to ν_{NH}, $\nu_{C=O}$ and $\nu_{C=N}$, and the NMR spectrum exhibited a broad signal (1H) exchanged with D_2O at τ 1·0, besides aromatic protons (13H). On the basis of the above spectral data and of the mass spectrum, it was deduced that **5a** is the benzoylhydrazone of 3-benzoylfuran. Indeed, **5a** was identical with a sample prepared from **4a** and benzoylhydrazine. The formation of **4a** can be viewed as proceeding by way of hydrazone **5a** since **5a** was easily hydrolysed with trace amounts of water into **4a** on heating or irradiation (Scheme 2).

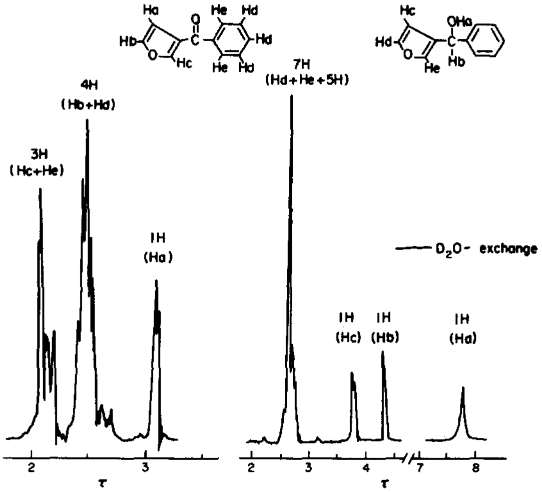


Fig 2. NMR spectra of **4a** and **6** in $CDCl_3$.

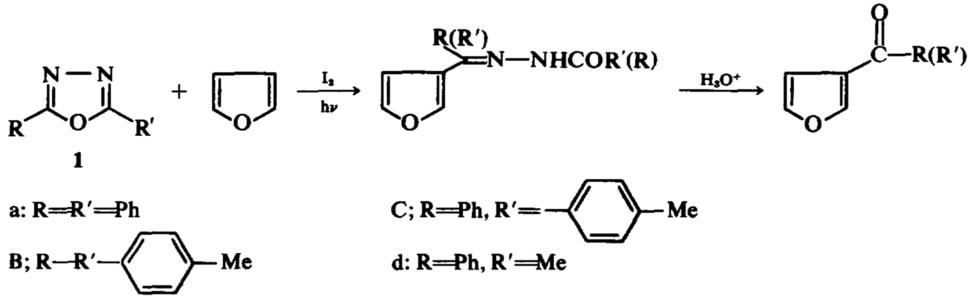
Similarly, the photochemical reactions of 2,5-di(*p*-tolyl)-1,3,4-oxadiazole (**1b**) with furan gave 3-*p*-toluylfuran (**4b**) and its hydrazone **5b**.

It might be expected that two isomers of the 3-acylfuran and of their hydrazones could be formed in a similar photochemical reaction of 1,3,4-oxadiazole having different substituents at the 2- and 5-positions.

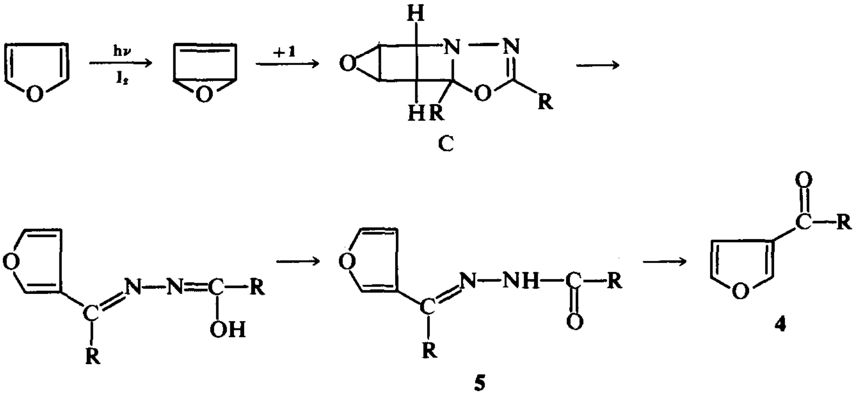
In the photochemical reaction of 2-phenyl-5-*p*-tolyl-1,3,4-oxadiazole (**1c**), equimolar amounts of **4a** and **4b** were obtained in low yield. On the other hand, the photochemical reaction of 2-methyl-5-phenyl-1,3,4-oxadiazole (**1d**) afforded **4a** and 3-benzoyl acetylhydrazone (**5d**); 3-acetylfuran and its benzoylhydrazone could not be detected in the products. The structures of **4b** and **5d** were confirmed by spectral data. And, **5d** was identical with an authentic sample prepared from **4a** and acetylhydrazine.

Pathway for the formation of hydrazone **5**. The fact that 2-benzoylfuran was not transformed into 3-benzoylfuran under the irradiation conditions, suggests that the bond between the carbon at the 3-position of furan and that a the 2-position of the 1,3,4-oxadiazole was formed selectively. Upon irradiation of oxadiazole **1a** in the presence of iodine, no ring opening was observed but a complex with iodine was obtained; which on treatment with $Na_2S_2O_4$, gave oxadiazole **1a** quantitatively.[5] It was also ascertained that photolysis of 1:1 cycloadduct **2** in the presence of iodine did not occur and **2** was recovered quantitatively.

On the basis of the above observations and of the results mentioned below, hydrazone **5** may be viewed as arising *via* cyclic intermediate C which



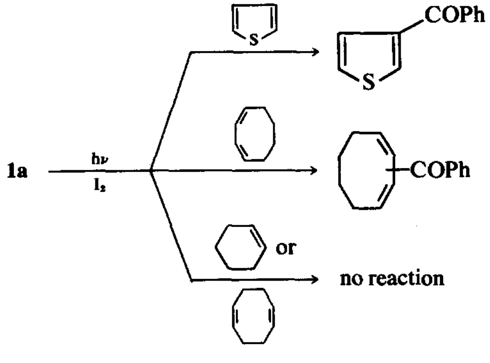
SCHEME 2



SCHEME 3

corresponds to the 1:1 cycloadduct of oxadiazole **1** to cyclobutadiene oxide (Scheme 3). Although its function in the photochemical reaction is not clear, iodine might play a role in the valence tautomerization of furan into cyclobutadiene oxide.

It might be expected that other cyclic conjugated dienes would give the corresponding acyl derivatives by the photochemical reaction with oxadiazole **1** in the presence of iodine. Indeed, 3-benzoylthiophene was isolated from the photolysis of **1a** in a benzene solution of thiophene. The photochemical reaction of oxadiazole **1a** with cyclohexene and 1,5-cyclooctadiene did not occur, while 1,3-cyclooctadiene, also a conjugated diene, afforded a benzoyl-1,3-cyclooctadiene.



Further extensions of the novel photo-induced acylation reaction is in progress.

EXPERIMENTAL

All m.p.'s are uncorrected. IR spectra were measured as KBr discs on a Nippon Bunko IR-S and the mass spectra were obtained on a Hitachi RMS-4 mass spectrometer (direct inlet, ionization energy 70 eV). NMR spectra were determined at 60 MHz with a Hitachi R-20 NMR spectrometer (TMS) and the microanalyses were performed by Miss M. Akita of our laboratory.

Irradiations were performed in an apparatus using 300W high-pressure mercury lamp (Taika HLV-B). Pyrex filters were used for all experiments and agitation was achieved by bubling dry N_2 through the reaction.

Materials. 2,5-Disubstituted 1,3,4-oxadiazoles were prepared by the method of Grekov *et al.*[6] and purified by recrystallization. 2,5-Diphenyl- (**1a**), m.p. 140–141° (lit.[7] m.p. 140°); 2,5-di(*p*-tolyl)- (**1b**), m.p. 174–175° (lit.[8] m.p. 175–176°); 2-phenyl-5-*p*-tolyl- (**1c**), m.p. 127–128° (lit.[8] m.p. 125–126°); 2-methyl-5-phenyl-1,3,4-oxadiazole (**1d**), m.p. 66–67° (lit.[8] m.p. 65–66°). Benzophenone was recrystallized from ether-petroleum and iodine was sublimated prior to use. Benzene, furan (b.p. 32°), thiophene (b.p. 84°), cyclohexene (b.p. 81–83°), 1,3-cyclooctadiene (b.p. 140–141°) and 1,5-cyclooctadiene (b.p. 147–149°) were freshly distilled before use.

Photochemical reaction of **1a** *with furan*

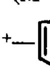
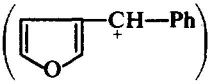
(*a*) *In the presence of benzophenone.* A soln of **1a** (0·90 g), furan (25 g) and benzophenone (0·18 g) in 400 ml benzene was irradiated under cooling with running water for 10 h, and then the mixture concentrated *in vacuo* to a residue. This was chromatographed on alumina using benzene as eluent to give 0·17 g (95%) of benzophenone and 0·31 g (26%) of **2**. Recrystallization of **2** from acetone afforded colorless prisms, m.p. 179–181°. (Found: C, 74·79; H, 4·41; N, 9·66. Calc. for $C_{18}H_{14}N_2O_2$: C, 74·94; H, 4·63; N, 9·57%). IR cm^{-1}: $\nu_{C=N}$ 1660, ν_{C-O-C} 1070. *m/e* 290 (M^+), 261 (M^+—CHO), 187 (M^+—PhCN), 157 (187^+—NO), 128 (157^+—CHO), 105 ($PhCO^+$), 77 (Ph^+).

Similarly reaction without benzophenone afforded 0·21 g (18%) of **2**.

(*b*) *In the presence of iodine.* A typical run is as follows. A solution of 2·2 g of **1a**, 60 g of furan and 0·50 g of iodine in 500 ml of benzene was irradiated under cooling with ice-water for 10 h: during which time the mixture became muddy. The mixture was concentrated *in vacuo* and the residue chromatographed on silica gel using $CHCl_3$ as eluent. From the first elution 0·17 g (10%) of 3-benzoylfuran (**4a**) was obtained as yellow viscous oil.[9] *m/e*: 172 ((M^+), 144 (M^+—CO), 115 (144^+—CHO), 105 ($PhCO^+$), 95 (M^+—Ph), 77 (Ph^+).

2,4-Dinitrophenylhydrazone of **4a**: m.p. 191–192°. (Found: C, 58·07; H, 3·34; N, 16·03. Calc. for $C_{17}H_{12}N_4O_5$: C, 57·95; H, 3·43; N, 15·90%.)

From the second and third elutions 1·10 g (50%) of unreacted **1a** and 60 mg (3%) of benzoylhydrazone (**5a**) of **4a** were isolated respectively. Recrystallization of **5a** from EtOH afforded colorless needles, m.p. 125–125°. (Found: C, 74·62; H, 5·10; N, 9·44. Calc. for $C_{18}H_{14}N_2O_2$:

C, 74·47; H, 4·86; N, 9·65%.) IR cm^{-1}: ν_{NH} 3320, $\nu_{C=N}$ 1660, $\nu_{C=O}$ 1675. NMR ($CDCl_3$) τ: 1·7–2·7 (13H, m, aromatic H), 1·0 (1H, s, N*H*, exchanged with D_2O). *m/e*: 290 (M^+), 273 (M^+—H_2O), 262 (M^+—N_2), 261 (M^+—CHO), 223 (M^+— ), 213 (M^+—Ph), 185 (M^+—PhCO), 157 (

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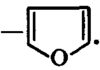
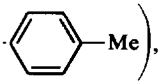
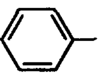
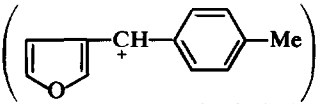
Hydrazone **5a** was identical with a sample prepared from **4a** and benzoylhydrazine in an usual manner.

In a similar photolysis of **1a** under cooling with running water, 16·5% of **4a** was obtained and **5a** was not isolated.

The yields of the corresponding 3-acylfurans **4** and fheir acylhydrazones **5** obtained from photolysis of other 1,3,4-oxadiazoles **1b–1d** were as follows. From **1b**, 3-toluylfuran (**4b**) 16·0% (under cooling with water); **4b** 5·4% and toluylhydrazone (**5b**) of **4b** 4·0%. From **1c**, 1:1 mixture of **4a** and **4b*** 2·0% (under cooling with water). From **1d**, **4a** 2·0% and acetylhydrazone (**5d**) of **4a** 3·0% (under cooling with water).

Hydrazone **5b**: m.p. 153°, colorless needles. (Found: C, 74·28; H, 5·47; N, 8·96. Calc. for $C_{20}H_{18}N_2O_2$: C, 74·45; H, 5·70; N, 8·80%.) IR cm^{-1}: ν_{NH} 3340, $\nu_{C=N}$ 1660, $\nu_{C=O}$ 1680. NMR ($CDCl_3$) τ: 7·5 (6H, s, CH_3) 1·9–2·8 (11H, m, aromatic H), 1·0 (1H, s, NH, exchanged with D_2O). *m/e*: 318 (M^+), 301 (M^+—OH), 290 (M^+—N_2), 289 (M^+—CHO), 251 (M^+— ), 250, 227 (M^+— 

), 199 (M^+—Me—  —CO), 171 (

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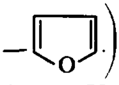
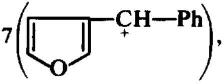
Hydrazone **5b** was identical with a sample prepared from **4b** and toluylhydrazine. Hydrazone **5d**: m.p. 120°, colorless needles. (Found: C, 68·61; H, 5·30; N, 12·08. Calc. for $C_{13}H_{12}N_2O_2$: C, 68·41; H, 5·30; N, 12·27%.) IR cm^{-1}: ν_{NH} 3300, $\nu_{C=N}$ 1670, $\nu_{C=O}$ 1690. NMR ($CDCl_3$) τ: 7·55 (3H, s, CH_3), 2·2–2·8 (8H, m, aromatic H), 1·25 (1H, s, NH, exchanged with D_2O). *m/e*: 228 (M^+), 186 (M^+—CH_2CO), 161 (M^+— ), 157 (

), 151 (M^+—Ph). Hydrazone **5d** was identical with a sample prepared from **4a** and acetylhydrazine.

Hydrogenation of **2**

A suspension of **2** (0·2 g) and 70 mg of Adams' catalyst of dioxane (30 ml) was stirred in a stream of H_2 at room temp. After 43 ml of H_2 had been absorbed dioxane was removed *in vacuo* to leave a residue, which was washed with 100 ml light petroleum. The washings were concentrated and several fractional recrystallizations of the residue from acetone afforded 80 mg of 1,3,4-oxadiazole **1a** and 20 mg of dihydro compound **3**, m.p. 180–181°, as colorless prisms. (Found: C, 73·75; H, 5·62; N, 9·54. Calc. for $C_{18}H_{16}N_2O_2$: C, 73·95; H, 5·52; N, 9·58%.) IR cm^{-1}: $\nu_{C=N}$ 1650, ν_{C-O-C} 1080.

NMR ($CDCl_3$) τ: 7·6–8·4 (2H, m, CH_2), 6·0–6·8 (2H, m, CH_2), 5·2–5·8 (1H, m, —CH), 3·13 (1H, unsymmetrical s, —CH), 2·0–2·9 (10H, m, aromatic H). *m/e*: 292 (M^+), 222 (**1a**$^+$), 189 (M^+—PhCN), 173 (M^+—PhCNO), 159 (189^+—NO), 146 (173^+—HCN), 130 (159^+—CHO), 105 ($PhCO^+$), 77 (Ph^+).

Reduction of 3-benzoylfuran (**4a**) *with sodium borohydride*

A soln of 0·2 g **4a** in EtOH (10 ml) was stirred with 0·1 g of $NaBH_4$ at room temp for 1 h. To the mixture was added 5 ml H_2O and the resulting mixture was heated at 60–80° for 3 h. Additional 50 ml H_2O was added and the soln extracted with ether 100 ml. The extract was concentrated to leave 0·2 g (100%) of crystals, which on recrystallization from light petroleum gave carbinol **5**, m.p. 65–65·5°, as colorless needles. (Found: C, 75·87; H, 5·88. Calc. for $C_{11}H_{10}O_2$: C, 75·84; H, 5·79%.) IR cm^{-1}: ν_{OH} 3140–3260. *m/e*: 174 (M^+), 157 (M^+—OH), 146 (M^+—CO), 145 (M^+—CHO), 128 (157^+—CHO), 117 (146^+—CHO), 105 ($PhCO^+$), 97 (M^+—Ph), 77 (Ph^+).

Photochemical reaction of **1a** *with thiophene in the presence of iodine*

A soln of 2·2 g of **1a**, 16·0 g of thiophene and 0·5 g of iodine in benzene (500 ml) was irradiated for 10 h under similar conditions to those described above. The mixture was concentrated *in vacuo* and the residue chromatographed on alumina using benzene as an eluent to give 0·2 g (10%) of crystals. Recrystallization from light petroleum gave 3-benzoylthiophene, m.p. 64·5° (lit.,[10] m.p. 63°), as colorless prisms. (Found: C, 70·13; H, 4·36. Calc. for $C_{11}H_8OS$: C, 70·21; H, 4·29%.) IR cm^{-1}: $\nu_{C=O}$ 1650. NMR ($CDCl_3$) τ: 2·0–2·7 (m, aromatic H). *m/e*: 188 (M^+), 166 (M^+—CO), 111 (M^+—Ph), 105 ($PhCO^+$).

Photochemical reaction of **1a** *with* 1,3-*cyclooctadiene in the presence of iodine*

A soln of 2·2 g of **1a**, 5·4 g of 1,3-cyclooctadiene and 0·5 g of iodine in 500 ml of benzene was irradiated for 40 h under similar conditions to those described above. The benzene was removed *in vacuo* to leave a residue, which was chromatographed on silica gel using $CHCl_3$ as eluent to afford 2·3 g of unreacted cyclooctadiene and 0·61 g (29%) of yellow oil. The oil was identified as 2,4-dinitrophenylhydrazone of a benzoyl-1,3-cycloocatdiene, m.p. 153–154°, as yellow needles. (Found: C, 64·06; H, 5·03; N, 14·04. Calc. for $C_{21}H_{20}N_4O_4$: C, 64·27; H, 5·14; N, 14·28%.)

REFERENCES

[1] O. Tsuge, M. Tashiro and K. Oe, *Tetrahedron Letters* 3971 (1968).

[2] G. O. Schenk, W. Hartmann and R. Steinmetz, *Chem. Ber.* **96**, 498 (1963); M. Ogata, H. Watanabe and H. Kano, *Tetrahedron Letters* 533 (1967).

[3] D. Gagnaire and E. Payo-Subiza, *Bull. Chim. Soc. France* 2623 (1963).

[4] W. Borsche and H. Leditschke, *Liebig Ann. Chem.*, **529**, 108 (1937).

[5] It has been reported that **1a** and bromine in acetic acid

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*Quantitative analysis was performed by gas chromatography.

or carbon tetrachloride gave a complex, which on treatment with aqueous ethanol afforded the original oxadiazole (O. P. Shvaika and G. P. Klimisha, *Zh. Obshch. Khim.*, **35** 290 (1965)).

[6] A. P. Grekov, L. N. Kulakova and O. P. Shvaika, *Zh. Obshch. Khim.*, **29**, 3054 (1959).

[7] R. Stolle, *Ber.*, **32**, 798 (1899).

[8] R. Huisgen, J. Sauer, H. J. Sturm and J. H. Markgraf, *Chem. Ber.*, **93**, 2106 (1960).

[9] P. Grunanger and A. Mantegani, *Gazz. Chim. Ital.* **89**, 913 (1959).

[10] B. R. Baker, R. E. Schaub, F. J. McEvoy and J. H. Williams, *J. Org. Chem.* **18**, 133 (1953).