

Fluorescence and Liquid Scintillation Properties of 1,3,4-Oxadiazoles. I.  
Excimer Formation in 2-Alkyl-5-(4-biphenyl)-1,3,4-Oxadiazoles.

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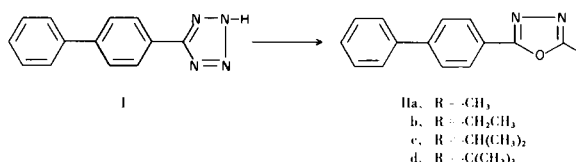
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Several 2-alkyl-5-(4-biphenyl)-1,3,4-oxadiazoles have been synthesized and investigated as primary liquid scintillation solutes and are found to be excellent fluors. Fluorescence studies at varying concentrations and temperatures indicate that excimer formation is possible at high concentration and low temperatures.

There has been long standing interest in derivatives of the 1,3,4-oxadiazole system as possible primary liquid scintillation solutes. Hayes investigated several aromatic systems incorporating the 1,3,4-oxadiazole ring and from this group of compounds one in particular, 2-(4-biphenyl)-5-phenyl-1,3,4-oxadiazole (PBD), was found to be a particularly good primary liquid scintillation solute having a reported pulse height relative (RPH) to a 3.0 g./l. solution of 2,5-diphenyloxazole (PPO) in toluene of 1.28 at a concentration of 10 g./l. in toluene (1,2). More recently, considerable interest has been shown in studies of the ultraviolet-excited fluorescence of these compounds, with particular emphasis on the formation of excited dimers (excimers) by PBD and also by 2,5-diphenyl-1,3,4-oxadiazole (PPD).

Excimer formation results from the association of an excited aromatic molecule in the singlet state with another of the same molecule in the ground state (3-6). This process competes with prompt fluorescence from an excited monomer and thus the fluorescence yield is affected, along with the wavelength distribution of emitted photons which is also altered since the excimer itself fluoresces at its own wavelength. The formation of excited dimers is affected by concentration, temperature and solvent. Thus, two methods are employed to determine whether or not a molecule is capable of excimer formation. First, the formation of excimer increases with increasing concentration with the appearance of a resulting long wavelength band which is due to the emission of the excimer. Second, one of the most conclusive ways of determining whether the appearance of a long wavelength band at high concentration is due to excimer formation or impurities is to investigate the effect of temperature changes on the distribution of photons (7,8).



Lami and Laustriat (9) concluded from theoretical considerations on the interaction between the ground state and first excited singlet state that PBD and PPD would be prevented from forming excimers since these two states have permanent dipole moments which are mutually repulsive. PBD is not a highly soluble compound, however, so Horrocks (10) investigated some highly soluble derivatives of PBD and found that these compounds do form excimers at high concentration and low temperature, although only to a small extent.

It was of interest then, for us to investigate 2-alkyl-5-(4-biphenyl)-1,3,4-oxadiazoles (II) (BD) for the possibility of excimer formation since they differ from the previously investigated PBD derivatives only by the substitution of an alkyl group for an aromatic moiety and from PPD only by the order of arrangement of the aromatic ring systems.

The BD derivatives investigated in this study are listed in Table I. The synthesis of these compounds was accomplished from 5-(4-biphenyl)-2H-tetrazole (I) according to the method outlined by Sauer (11) for 1,3,4-oxadiazoles in general. In order to establish the unambiguity of Sauer's method, one compound, IIa, was also synthesized from 4-biphenylcarboxylic acid according to the general method previously described by Hayes (12).

Purification of the BD derivatives was accomplished by repeated recrystallization from cyclohexane or ethanol followed by chromatography through an alumina column

TABLE I  
Physical Data for 2-Alkyl-5-(4-biphenyl)-1,3,4-oxadiazoles

Compound	M.p., °C	fluorescence max, (nm)	absorption max, (nm)	log $\epsilon$	RPH (a)	C <sub>max</sub> , g./l. (b)
IIa	155-156	336	284	4.45	0.93 (c) (1.18) (d) (0.98) (e)	5.0 6.7
IIb	122-123	336	284	4.49	1.00 (e)	10.0
IIc	107-108	336	284	4.40	1.03 (e)	13.3
II d	112-113	336	284	4.47	1.05 (e)	15.0

(a) Relative to 3.0 g./l. of 2,5-diphenyloxazole in toluene. (b) Concentration at which maximum relative pulse height reached. (c) One ml. aerated solution, Bi<sup>207</sup> excitation. (d) One ml. deaerated solution, Bi<sup>207</sup> excitation. (e) Fifteen ml. aerated solution, H<sup>3</sup> excitation.

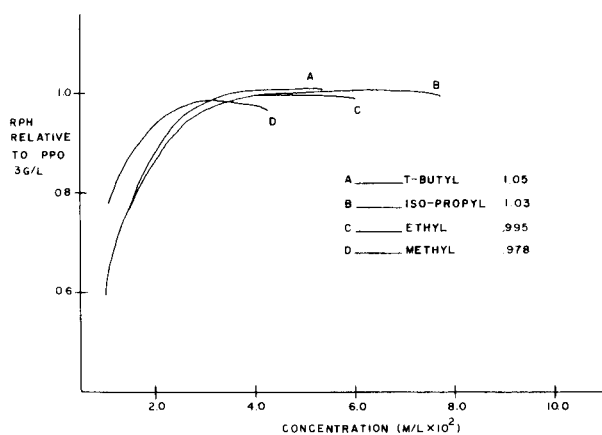


Figure 1. Plot of relative fluorescence intensity versus wavelength for 2-(4-biphenyl)-5-methyl-1,3,4-oxadiazole (IIa) at various concentrations.

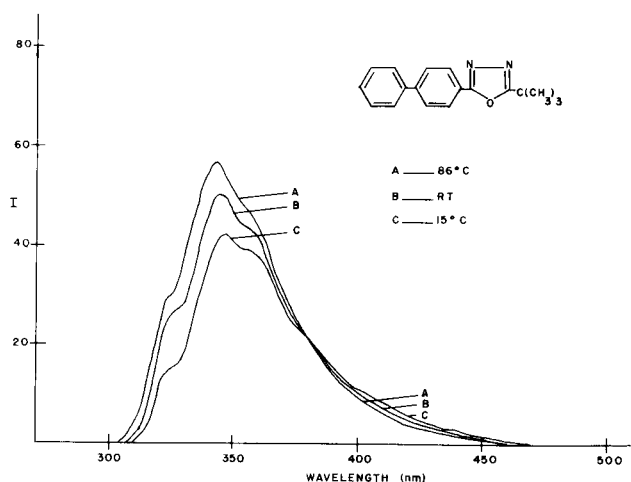


Figure 2. Plot of relative fluorescence intensity versus wavelength for 2-(4-biphenyl)-methyl-1,3,4-oxadiazole (IIa) at room temperature and 70°.

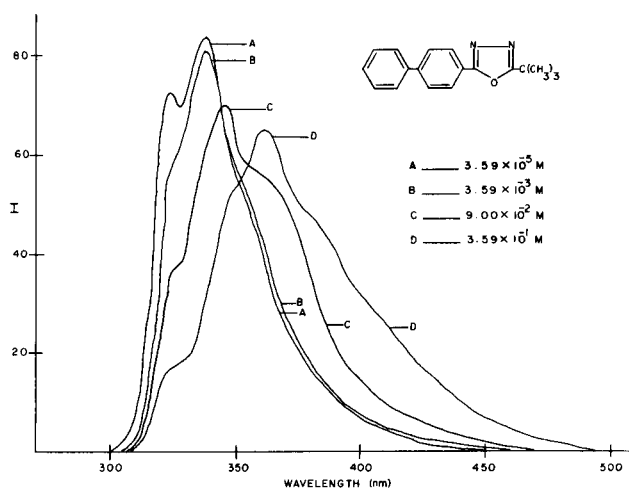


Figure 3. Plot of relative fluorescence intensity versus wavelength for 2-(4-biphenyl)-5-*t*-butyl-1,3,4-oxadiazole (II d) at various concentrations.

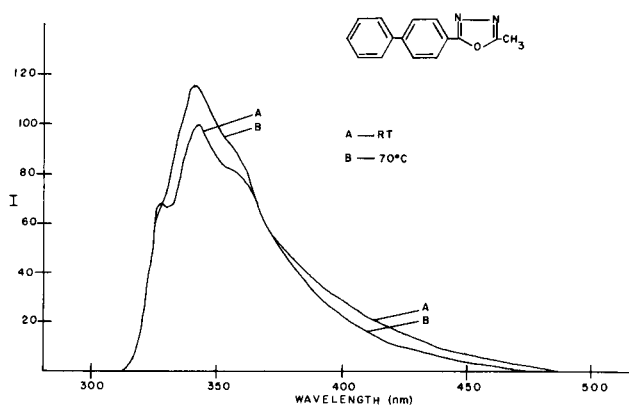


Figure 4. Plot of relative fluorescence intensity versus wavelength for 2-(4-biphenyl)-5-*t*-butyl-1,3,4-oxadiazole (II d) at 15° and 86°.

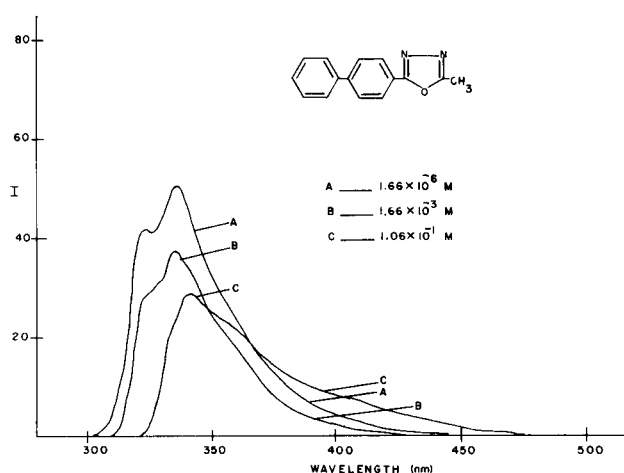


Figure 5. Relative pulse height curves for 2-alkyl-5-(4-biphenyl)-1,3,4-oxadiazoles.

in cyclohexane or benzene. All compounds were extensively purified before study. All compounds gave a correct carbon and hydrogen analysis and were found to be homogeneous by thin-layer chromatography on Mallinckrodt SILICAR TLC-7GF using a 10-90 mixture (by volume) of diethyl ether-methylene chloride as a developing solvent. Impurities appear as either fluorescent or black spots against the fluorescent background under a short wavelength ultraviolet lamp.

Fluorescence measurements were made using a Farrand MK-1 spectrofluorimeter with slits giving a 0.5 nm band-pass. Spectra were determined in Eastman spectro grade cyclohexane using solutions which were saturated with nitrogen to remove air present, either in closed 1 mm quartz capillaries or a triangular quartz cuvette. In either case, distortions of the spectra due to self-absorption were minimized. Spectra were run at various concentrations and at three different temperatures. All spectra are corrected for response of the phototube.

Since both PBD and PPD are excellent liquid scintillation solutes it was of interest to investigate the BD derivatives prepared for their performance as primary liquid scintillation solutes as well. One compound, 2-(4-biphenyl)-5-methyl-1,3,4-oxadiazole (IIa) was tested as a primary liquid scintillation solute in two ways. The scintillation performance relative to a 3.0 g./l. solution of 2,5-diphenyloxazole (PPO) was first determined for IIa by irradiating a 1 ml. toluene solution of this compound with a  $\text{Bi}^{207}$  excitation source. The scintillation was observed with a RCA 6903 quartz-face photomultiplier having average S-13 spectral characteristics. Solutions were counted under both air equilibrated and deaerated conditions. A detailed description of the testing apparatus has been previously reported (13).

Compound IIa and the other BD derivatives were also evaluated as primary solutes using a Packard 3310 liquid scintillation counter according to a procedure devised by Gibbs (14). Fifteen ml. of a 3.0 g./l. solution of PPO and 15 ml. of the compound to be tested in glass sample vials spiked with 100,000 dpm of tritiated toluene and were placed in the sample chamber. The windows were set from lower to infinity and the lower discriminator was set at 1000. The upper discriminator is inoperative. The gain was adjusted to give 1000 cpm with the PPO sample. The sample of interest was then moved into the counting chamber and the lower discriminator is then adjusted to give a reading of 1000 cpm. If the RPH value is less than PPO, it is read directly from the dial. If the RPH for the unknown is greater than PPO, it is necessary to use the gain adjustments rather than the lower discriminator. The gain adjustment necessary to give 1000 cpm for the unknown compound is determined and the ratio of gain for the unknown over the gain for PPO gives a RPH value. All samples were counted under air-equilibrated conditions using Packard glass counting vials.

In view of the fact that both previously investigated linear aromatic systems containing the 1,3,4-oxadiazole ring system did not form excimers, or that they did so only to a slight extent, it is interesting to note that all of the BD derivatives examined in this report form excimers readily, even at room temperature. Figure 1 shows the fluorescence spectrum of methyl-BD (IIa) as a function of concentration. At low concentration ( $1.66 \times 10^{-6}$  molar) there is no distortion of the distribution of photons toward longer wavelengths, but a concentration at  $1.06 \times 10^{-1}$  molar the fluorescence at longer wavelengths increases relative to the normal monomer emission. As an indication of excimer formation in IIa, Figure 2 shows that the long wavelength component is temperature dependent with a decrease of excimer emission relative to monomer fluorescence at higher temperatures. The methyl-BD (IIa) forms excimers more easily than does the methyl-PBD derivatives that Horrocks (10) studied.

The *t*-butyl BD (IIc) was also examined for excimer formation at various concentrations and temperatures (Figures 3 and 4). It was felt that the bulky *t*-butyl group might sterically inhibit the formation of the excited dimer, but there is little difference between IIa and IIc in excimer formation.

The BD-derivatives have been found to be excellent primary liquid scintillation solutes, both when evaluated by  $\text{Bi}^{207}$  and tritium excitation. Compound IIa, which was tested under aerated and deaerated conditions was found to be subject to severe oxygen quenching, losing about twenty-five percent of the scintillation under aerated conditions. All of the BD derivatives exhibited relatively little concentration quenching, even with the large volume

(15 ml.) used in many of the runs. It is interesting to note that the more highly substituted derivatives show (Figure 5) much less concentration quenching in a 15 ml. volume than does the methyl derivative IIa. Compound IIa reaches a maximum relative pulse height at about 6.7 g./l. ( $2.84 \times 10^{-2} M$ ), IIb at 10 g./l. ( $4 \times 10^{-2} M$ ), IIc at 13.3 g./l. ( $4.85 \times 10^{-2} M$ ), and finally IId at 15 g./l. ( $5.2 \times 10^{-2} M$ ). The *t*-butyl derivative, IId, was also the best primary solute of the series with a maximum relative pulse height of 1.05.

The alkyl BD derivatives all exhibit ultraviolet absorption maxima at 284 nm in cyclohexane (Table I) which is about the same as is reported for isomeric PPD compounds (15,16). On our instrument we found a maximum of 285 nm in ethanol for *t*-butyl PPD, very close to the 284 nm obtained for IId. However, the BD derivatives fluoresce at somewhat shorter wavelengths than the PPD derivatives. Kowalski (16) reports a fluorescence maximum of 360 nm (in toluene) for both PPD and *t*-butyl PPD while Berlman (17) reports a maximum of 346 nm for PPD in cyclohexane. Using our spectrofluorimeter, we obtained values of 342 nm for PPD, 349 nm for *t*-butyl PPD and 336 nm for all of the BD derivatives. Thus the *t*-butyl BD shows a hypsochromic shift of the fluorescence maximum of 13 nm from the isomeric *t*-butyl PPD whereas the absorption maxima are nearly identical.

#### EXPERIMENTAL

All melting points reported were determined with a Thomas-Hoover melting point apparatus and are uncorrected. The microanalyses were performed by Huffman Laboratories, Wheat Ridge, Colorado. Ultraviolet absorption spectra were determined in spectrograde cyclohexane in a 1 cm quartz cuvette with a Beckman DU-2 spectrophotometer at concentration of about  $10^{-5}$  molar. Compounds IIa-IIc were prepared by refluxing two moles of the appropriate acid anhydride with the tetrazole I. Compound IId was prepared by refluxing two moles of pivaloyl chloride with I in dry pyridine. The work-up of the reaction product was similar in each case.

#### 4-Biphenyl-2H-tetrazole (I).

Twenty-five g. (0.140 mole) of 4-biphenylcarbonitrile (Eastman Kodak No. 6338), 11.9 g. (0.38 mole) of lithium chloride and 18.2 g. (0.28 mole) of sodium azide were mixed with 200 ml. of 2-methoxyethanol, were refluxed with stirring for 72 hours. After cooling, the reaction mixture was poured into 500 ml. of water and the product precipitated by the slow addition of concentrated hydrochloric acid. The precipitate was dried, and recrystallized from methanol to give 30.2 g. (97%) of compound I, which decomposed at 238-239°.

*Anal.* Calcd. for  $C_{13}H_{10}N_4$ : C, 70.26; H, 4.54. Found: C, 69.97; H, 4.61.

#### 2-(4-Biphenyl)-5-*t*-butyl-1,3,4-oxadiazole (IId).

Five g. (0.0225 mole) of 4-biphenyl-2H-tetrazole (I) were added to a solution of 5.9 g. (0.049 mole) of pivaloyl chloride in 120 ml. of dry pyridine. The reaction mixture was refluxed for one hour, cooled and poured into water. The precipitate was filtered, dried and recrystallized from 60-90° petroleum ether to afford 4.2 g. (66%) of IId, m.p. 112-113°. Repeated recrystallizations from petroleum ether and ethanol with column chromatography

through alumina in petroleum ether gave an analytical sample, m.p. 112.5-113.5°.

*Anal.* Calcd. for  $C_{18}H_{18}N_2O$ : C, 77.67; H, 6.52. Found: C, 77.66; H, 6.68.

#### 2-(4-Biphenyl)-5-methyl-1,3,4-oxadiazole (IIa).

This compound was obtained in 46% yield, m.p. 155-156°.

*Anal.* Calcd. for  $C_{15}H_{12}N_2O$ : C, 76.24; H, 5.12. Found: C, 76.02; H, 5.20.

#### 2-(4-Biphenyl)-5-ethyl-1,3,4-oxadiazole (IIb).

This compound was obtained in 73% yield, m.p. 121.5-123°.

*Anal.* Calcd. for  $C_{16}H_{14}N_2O$ : C, 76.78; H, 5.64. Found: C, 76.73; H, 5.58.

#### 2-(4-Biphenyl)-5-isopropyl-1,3,4-oxadiazole (IIc).

This compound was obtained in 59% yield, m.p. 107-108.5°.

*Anal.* Calcd. for  $C_{17}H_{16}N_2O$ : C, 77.25; H, 6.10. Found: C, 76.95; H, 5.98.

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