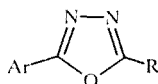


¹H AND ¹³C NMR SPECTRA OF 1,5-DISUBSTITUTED 1,3,4-OXADIAZOLES

I. S. Poddubnyi, L. I. Belen'kii, M. I. Struchkova,
and M. M. Krayushkin

The ¹H and ¹³C NMR spectra of 2,5-disubstituted 1,3,4-oxadiazoles with aliphatic, aromatic, and hetero-aromatic substituents have been described and interpreted. The electronic effect of the 1,3,4-oxadiazole group as a benzene ring substituent was evaluated using ¹³C NMR spectroscopy.

There have been only a few references to the ¹H and ¹³C NMR spectra of 2,5-disubstituted 1,3,4-oxadiazoles [1-8] and complete signal assignment was not carried out in any of the cited works. A large set of such compounds has been obtained in our laboratory, in which one substituent is an aryl group and the other (R) is an alkyl (Ia-Ic), aryl (IIa-IIr), or heteryl substituent (IIIa-IIIn), from trichloromethylarenes and acylhydrazines [9].



Ia-c R = Me, a Ar = Ph, b Ar = 2,4,5-Me₃C₆H₂, c Ar = Ar = 2,4-Me₂C₆H₃, IIa-e Ar = Ph, a R = Ph, b R = 2-HOC₆H₄, c R = 2-O₂NC₆H₄, d R = 3-O₂NC₆H₄, e R = 4-O₂NC₆H₄, f R = 3-BrC₆H₄, g R = 2,4-Me₂C₆H₃, h R = 2,4,5-Me₃C₆H₂, i-l Ar = 2,4-Me₂C₆H₃, i R = 2-HOC₆H₄, j R = 2-O₂NC₆H₄, k R = 3-O₂NC₆H₄, l R = 4-O₂NC₆H₄, m-p Ar = 2,4,5-Me₃C₆H₂, m R = 2-HOC₆H₄, n R = 2-O₂NC₆H₄, o R = 3-O₂NC₆H₄, p R = 4-O₂NC₆H₄, q,r Ar = 2,3,4,5-Me₄C₆H, q R = 3-O₂NC₆H₄, r R = 2-HOC₆H₄, IIIa-d Ar = Ph, a R = 4,5-dibromo-2-furyl, b R = 2-thienyl, c R = 3-pyridyl, d R = 4-pyridyl, e Ar = 3-BrC₆H₄, R = 4-pyridyl, f-i Ar = 2,4-Me₂C₆H₃, f R = 4,5-dibromo-2-furyl, g R = 2-thienyl, h R = 3-pyridyl, i R = 4-pyridyl, j-m Ar = 2,4,5-Me₃C₆H₂, j R = 4,5-dibromo-2-furyl, k R = 2-thienyl, l R = 3-pyridyl, m R = 4-pyridyl, n Ar = 2,3,4,5-Me₄C₆H, R = pyridyl

In the present work, we analyzed the ¹H and ¹³C NMR spectra of oxadiazoles obtained in our laboratory (including Ib, Ic, IIe-IIr, IIIa, and IIIe-n, which are reported for the first time) as well as spectra given in the literature. The spectral data for the compounds synthesized are given in Tables 1 and 2.

An examination of the PMR spectra shows that the 1,3,4-oxadiazole ring is an electron-withdrawing substituent in the benzene ring with an *-i, -m* effect, which is reminiscent of acyl groups. The PMR spectra parameters of 2,5-diphenyl-1,3,4-oxadiazole IIa are virtually identical to the data given by Tashtoush et al. [8]. We should note that the unusual broadening of the 2'-H, 5'-H, and 6'-H protons of the pyridine ring in oxadiazole IIIh (in CDCl₃) probably is not related either to quadrupole coupling of the nitrogen atom with the protons or possible rotation of the pyridine ring relative to the C—C bond

connecting the pyridine and oxadiazole rings since such broadening is not found in the spectra of IIIc, IIIId, IIIi, IIIl, and IIIm, which contain 3- and 4-pyridyl fragments. This broadening is probably the consequence of intermolecular interactions as indirectly indicated by its disappearance when deuteriochloroform is replaced as the solvent by DMSO- d_6 .

The signal assignment for nitrophenyl-, hydroxyphenyl-, and 3-bromophenyloxadiazoles was carried out using the substituent increments for substituted benzenes and the following equation

$$\delta_{H_j} = 7.26 + \sum_{j=1}^n \Delta\delta_j \quad (1)$$

where 7.26 is the chemical shift of the protons of unsubstituted benzene in $CDCl_3$ or CCl_4 (ppm) and $\Delta\delta_j$ is the increment of the corresponding substituent (ppm). 2,5-Diphenyl-1,3,4-oxadiazole IIa was taken as the model compound for calculating the increments of the oxadiazole ring. The following increments were obtained for the 1,3,4-oxadiazole ring (ppm):

$$\begin{aligned} \Delta\delta_o &= 8.13 - 7.26 = 0.87 \\ \Delta\delta_m \sim \Delta\delta_p &= 7.53 - 7.26 = 0.27 \end{aligned}$$

The best agreement of the chemical shifts of the protons of disubstituted benzenes calculated using the additive scheme is observed for the meta and para derivatives. The virtual agreement of the chemical shifts of the protons in the meta and para position of the benzene rings of diphenyloxadiazole IIa and 2-phenyl-5-R-1,3,4-oxadiazoles IIb-IIh and IIIa-IIIId may be attributed to predominance of the inductive effect of the 1,3,4-oxadiazole ring, while the conjugation effect is negligible. The lack of importance of conjugation is probably related to the noncoplanarity of diaryloxadiazoles IIa-IIh and 2-aryl-5-heteroxyloxadiazoles IIIa-IIIId. For example, an electron diffraction study showed that the dihedral angles between the plane of the oxadiazole ring and planes of the benzene rings in free IIa are $45 \pm 6^\circ$ [12]. The expansion of these angles upon the introduction of substituents at the ortho positions of the benzene rings presumably does not alter the contribution of the inductive effect.

Examination of the ^{13}C NMR spectra of I-III shows that the chemical shifts for the carbon atoms of the benzene ring in 5-R-2-phenyl-1,3,4-oxadiazoles hardly change (mostly in the range from 0.1 to 0.6 ppm) in going from R = Me (Ia) or Ph (IIa) to R = heteryl (IIIa-IIIId) or di-, tri-, and tetrasubstituted phenyl (IIb-IIh). The greatest changes are found for the ipso and para atoms [up to 1 ppm in the case of *p*- C_{6H_5} in 5-(4-nitrophenyl)-2-phenyl-1,3,4-oxadiazole]. The same behavior is observed not only for phenyl but other substituents if we consider them as the "standard" fragment in a series of compounds, in which the substituent changes in only one position of the oxadiazole ring. The changes in the chemical shifts of the para and ipso carbon atoms of the "standard" substituent are also the most marked in these cases [up to 1.2 ppm for the para atoms in 2-(2,4,5-trimethylphenyl)-5-R-1,3,4-oxadiazoles in going from R = Me to R = 4- $O_2NC_6H_4$]. This behavior indicates, on one hand, that the electronic interaction of the substituents at $C_{(2)}$ and $C_{(5)}$ of the oxadiazole ring is slight and is leveled off by this ring, which is a sort of a "buffer" aromatic system with its own pronounced electron-withdrawing effect. Furthermore, this behavior supports the abovementioned conclusion concerning the predominant role of the inductive effect of the oxadiazole ring due to the noncoplanarity of these molecules. On the other hand, the slight scatter of the chemical shifts of the carbon atoms of the "standard" substituents permits the rather facile assignment of the ^{13}C NMR signals for a series of monotypical substituted oxadiazoles if this assignment is carried out for at least one representative of this series.

2,5-Diphenyl-1,3,4-oxadiazole IIa was taken as the model compound for interpreting the ^{13}C NMR spectra as for the 1H NMR spectra. The substituent increments for substituted benzenes [11, 13] in $CDCl_3$ and CCl_4 were also taken into account. The chemical shifts of the pyridine carbon atoms, according to Ionin et al. [11], were taken equal to 150.6 ($C_{(2)}$), 124.5 ($C_{(3)}$), and 136.4 ppm ($C_{(4)}$). The following equation was used to calculate the chemical shifts of the benzene ring carbon atoms:

$$\delta_{C_j} = 128.5 + \sum_{j=1}^n \Delta\delta_j \quad (2)$$

where 128.5 is the chemical shift of the carbon atoms in benzene in $CDCl_3$ or CCl_4 (ppm) and $\Delta\delta_j$ is the substituent increment for monosubstituted benzenes (ppm).

The calculated increments for the 5-phenyl-1,3,4-oxadiazol-2-yl fragment as a substituent on the benzene ring, which were used for other 5-R-1,3,4-oxadiazol-2-yl fragments, are: $\Delta\delta_i = -4.8$ ($C_{(1)}$), $\Delta\delta_o = -1.8$ ($C_{(2)}$ and $C_{(6)}$), $\Delta\delta_m = 0.4$ ($C_{(3)}$)

TABLE 1. ¹H NMR Spectra of 2-Ar-R-Substituted Oxadiazoles I-III

Compound	Chemical shifts, ppm, coupling constants (J, Hz)			
	Ar ^{1,2}			R ³
	2-H (Me)/6-H	3-H (Me)/5-H (Me)	4-H (Me)	
1	2	3	4	5
Ia	Ph: 8,00 m	7,47 m	7,47 m	Me: 2,50 s
Ib	2,4,5-Me ₃ C ₆ H ₂ : (2,60)/7,67 s	7,08 s / (2,28)	(2,28)	Me: 2,60 s
Ic	2,4-Me ₂ C ₆ H ₃ : (2,82)/7,75 d	7,11 s / 7,08 d	(2,34)	Me: 2,56 s
IIa	Ph: 8,13 m	7,53 m	7,53 m	Ph: 8,13 m 7,53 m
IIb	Ph: 8,15 m	7,57 m	7,57 m	2-HOC ₆ H ₄ : 3'-H — 7,16 d.d. 4'-H — 7,47 d.d.d. , 5'-H — 7,05 d.d.d. 6'-H — 7,87 d.d. , OH-10,20 s
IIc	Ph: 8,08 m	7,55 m	7,55 m	2-O ₂ NC ₆ H ₄ : 3'-H — 8,12 m, 4'-H and 5'-H — 7,80 m, 6'-H — 8,07 m
IId	Ph: 8,13 m	7,54 m	7,54 m	3-O ₂ NC ₆ H ₄ : 2'-H — 8,90 d.d. , 4'-H — 8,48 d.d.d. , 5'-H — 7,74 τ, 6'-H — 8,38 d.d.d.
IIe	Ph: 8,16 m	7,57 m	7,57 m	4-O ₂ NC ₆ H ₄ : 2'-H, 6'-H — 8,41 m 3'-H and 5'-H — 8,34 m
IIf	Ph: 8,13 m	7,55 m	7,55 m	3-BrC ₆ H ₄ : 2'-H — 8,27 d.d. 4'-H — 7,67 d.d.d. , 5'-H — 7,41 τ, 6'-H — 8,08 d.d.d. (J ₂₁ = 1,9, J ₂₆ = 1,7, J ₄₅ = J ₅₆ = 8,0, J ₄₆ = 1,1)
IIg	Ph: 8,13 m	7,54 m	7,54 m	2,4-Me ₂ C ₆ H ₃ : 3'-H — 7,18 s, 5'-H — 7,16 d, 6'-H — 7,93 d (J ₅₆ = 8,0), 2'-Me — 2,74 s, 4'-Me — 2,40 s
IIh	Ph: 8,16 m	7,56 m	7,56 m	2,4,5-Me ₃ C ₆ H ₂ : 3'-H — 7,14 s, 6'-H — 7,82 s, 2'-Me — 2,71 s, 4'-Me — 2,33 s, 5'-Me — 2,31 s
IIi	2,4-Me ₂ C ₆ H ₃ : (2,74)/7,92 d	7,18 br.s 7,16 br.s	(2,40)	2-HOC ₆ H ₄ : 3'-H — 7,13 d.d. , 4'-H — 7,44 d.d.d. , 5'-H — 7,03 d.d.d. 6'-H — 7,82 d.d. OH — 10,2 s
IIj	2,4-Me ₂ C ₆ H ₃ : (2,68)/7,83 d	7,17 br.s 7,15 d	(2,39)	2-O ₂ NC ₆ H ₄ : 3'-H — 8,11 d.d. 4'-H and 5'-H — 7,77 m. 6'-H — 8,02 d.d.
IIk	2,4-Me ₂ C ₆ H ₃ : (2,71)/7,91 d	7,17 br.s /7,15 d	(2,39)	3-O ₂ NC ₆ H ₄ : 2'-H — 8,87 d.d. , 4'-H — 8,46 d.d.d. , 5'-H — 7,74 τ, 6'-H — 8,37 d.d.d.
IIl	2,4-Me ₂ C ₆ H ₃ : (2,76)/7,95 d	7,21 br.s / 7,19 d	(2,42)	4-O ₂ NC ₆ H ₄ : 2'-H, 6'-H — 8,32 m, 3'-H and 5'-H — 8,40 m
IIm	2,4,5-Me ₃ C ₆ H ₂ : (2,68)/7,77 s	7,10 s / (2,28)	(2,31)	2-HOC ₆ H ₄ : 3'-H — 7,13 d.d. , 4'-H — 7,44 d.d.d. , 5'-H — 7,03 d.d.d. 6'-H — 7,82 d.d. , OH — 10,26 s
IIn	2,4,5-Me ₃ C ₆ H ₂ : (2,63)/7,73 s	7,13 s / (2,30)	(2,30)	2-O ₂ NC ₆ H ₄ : 3'-H — 8,11 d. d. , 4'-H, 5'-H — 7,77 m, 6'-H — 8,02 d.d.
IIo	2,4,5-Me ₃ C ₆ H ₂ : (2,71)/7,82 s	7,16 c / (2,33)	(2,36)	3-O ₂ NC ₆ H ₄ : 2'-H — 8,94 d.d. , 4'-H — 8,51 d.d.d. , 5'-H — 7,77 τ, 6'-H — 8,41 d.d.d.
IIp	2,4,5-Me ₃ C ₆ H ₂ : (2,72)/7,82 s	7,16 s / (2,33)	(2,35)	4-O ₂ NC ₆ H ₄ : 2'-H, 6'-H — 8,33 m, 3'-H and 5'-H — 8,41 m
IIq	2,3,4,5-Me ₄ C ₆ H: (2,68)/7,63 s	(2,36)/ (2,33)	(2,42)	3-O ₂ NC ₆ H ₄ : 2'-H — 8,97 d.d. 4'-H — 8,54 d.d.d. , 5'-H — 7,79 τ, 6'-H — 8,44 d.d.d.
IIr	2,3,4,5-Me ₄ C ₆ H: (2,64)/7,58 s	(2,31)/ (2,29)	(2,37)	2-HOC ₆ H ₄ : 3'-H — 7,16 d.d. , 4'-H — 7,46 d.d.d. , 5'-H — 7,03 d.d.d. , 6'-H — 7,82 d.d. OH — 10,26 s

TABLE 1 (continued)

1	2	3	4	5
IIIa	Ph: 8,10 m	7,54 m	7,54 m	4,5-Br ₂ -2-C ₄ HO: 3'-H — 7,26 s
IIIb	Ph: 8,16 m	7,56 m	7,56 m	2-C ₄ H ₃ S: 3'-H — 7,83 d.d, 4'-H — 7,19 d.d, 5'-H — 7,57 d.d.
IIIc	Ph: 8,14 m	7,55 m	7,55 m	3-C ₅ H ₄ N: 2-H' — 9,36 d, 4'-H — 8,43 d.d.d 5'-H — 7,49 d.d, 6'-H — 8,78 d.d.
III d	Ph: 8,12 m	7,54 m	7,54 m	4-C ₅ H ₄ N: 2'-H and 6'-H — 8,82 m, 3'-H and 5'-H — 7,97 m
IIIe	3-BrC ₆ H ₄ : 8,30 d d/8,11 d.d.d (<i>J</i> ₂₄ = 1,9, <i>J</i> ₂₆ = 1,7, <i>J</i> ₄₆ = 1,1, <i>J</i> ₄₅ = - <i>J</i> ₅₆ = 8,0)	— / 7,45 τ	7,73 d d.d	4-C ₅ H ₄ N: 2'-H, 6'-H — 8,87 m, 3'-H and 5'-H — 8,00 m
III f	2,4-Me ₂ C ₆ H ₃ : (2,71)/7,88 d	7,17 s / 7,15 d	(2,40)	4,5-Br ₂ -2-C ₄ HO: 3'-H — 7,23 s
III g	2,4-Me ₂ C ₆ H ₃ : (2,71)/7,88 d	7,16 s / 7,14 d	(2,38)	2-C ₄ H ₃ S: 3'-H — 7,81 d 4'-H — 7,14 d.d, 5'-H — 7,56 d.
III h	2,4-Me ₂ C ₆ H ₃ : (2,72)/7,91 d	7,17 br. c/7,15 d	(2,39)	3-C ₅ H ₄ N: 2-H' — 9,35 br.s, 4'-H — 8,42 d 5'-H — 7,49 br.s, d, 6'-H — 8,78 d.d (<i>J</i> ₄₅ = 8,0, <i>J</i> ₅₆ = 4,9)
IIIh ³	2,4-Me ₂ C ₆ H ₃ : (2,65)/7,94 d	7,26 br.s 7,23 d	(2,36)	3-C ₅ H ₄ N: 2-H' — 9,26 s, 4'-H — 8,43 br.s 5'-H — 7,64 br., d.d, 6'-H — 8,80 br. (<i>J</i> ₄₅ = 8,0, <i>J</i> ₅₆ = 4,9)
IIIi	2,4-Me ₂ C ₆ H ₃ : (2,71)/7,91 d	7,16 s / 7,14 d	(2,38)	4-C ₅ H ₄ N: 2'-H, 6'-H — 8,81 m, 3'-H, 5'-H — 7,96 m
III j	2,4,5-Me ₃ C ₆ H ₂ : (2,65)/7,73 s	7,10 s / (2,28)	(2,28)	4,5-Br ₂ -2-C ₄ HO: 3'-H — 7,21 s
IIIk	2,4,5-Me ₃ C ₆ H ₂ : (2,67)/7,75 s	7,09 s / (2,28)	(2,30)	2-C ₄ H ₃ S: 3'-H — 7,80 d.d, 4'-H — 7,17 d.d, 5'-H — 7,54 d.d
III l	2,4,5-Me ₃ C ₆ H ₂ : (2,69)/7,70 s	7,13 s / (2,30)	(2,32)	3-C ₅ H ₄ N: 2-H' — 9,35 d 4'-H — 8,43 d.d.d, 5'-H — 7,49 d.d, 6'-H — 8,78 d.d
III m	2,4,5-Me ₃ C ₆ H ₂ : (2,68)/7,79 s 7,13 s / (2,30)	7,13 s / (2,30)	(2,32)	4-C ₅ H ₄ N: 2'-H and 6'-H — 8,82 m, 3'-H and 5'-H — 7,97 m
III n	2,3,4,5-Me ₄ C ₆ H: 1 (2,66)/7,60 s	(2,34) / (2,31)	(2,38)	4-C ₅ H ₄ N: 2'-H and 6'-H — 8,86 m, 3'-H and 5'-H — 8,01 m

*In all cases, the signals for the Me and OH substituents appear as singlets.

² *J*₅₆ = 8.0 Hz for Ic, Iii-III, and III d-IIIi.

³ For IIb, Iii, IIm, and IIr, *J*₃₄ = 8.4, *J*₃₅ = 1.1, *J*₄₅ = 7.2, *J*₅₆ = 7.8, and *J*₄₆ = 1.8 Hz, for IId, IIk, IIp, and IIq *J*₂₄ = 1.8, *J*₄₅ = *J*₅₆ = 8.0, *J*₂₆ = 2.2, *J*₄₆ = 1.0 Hz, for IIIb, IIIh, IIIk *J*₃₄ = 3.8, *J*₄₅ = 5.0, *J*₃₅ = 1.1 Hz, for IIj, II n *J*₃₄ = 7.1, *J*₅₆ = 7.3, *J*₄₆ = 1.9, *J*₃₅ = 1.0 Hz, for IIIc, III l *J*₄₅ = 8.0, *J*₅₆ = 4.9, *J*₄₆ = 1.7, *J*₂₄ = 2.2 Hz.

⁴ Spectrum taken in DMSO-d₆.

and C₍₅₎, and $\Delta\delta_p = 3.0$ ppm (C₍₄₎). In this case, the identification of the signals for *ipso* (quaternary) atom and the *para* carbon atom was not difficult, while the assignment of the meta and ortho atoms was carried out by comparing the chemical shifts of the model compound with the data for 2-(4,5-dibromofuryl)-5-phenyl- (IIIa) and 2-thienyl-5-phenyl-1,3,4-oxadiazoles (IIIb). The interpretation of the spectra of IIIa and IIIb was carried out using heteronuclear double resonance. This assignment was supported indirectly by the good agreement of the chemical shifts for 2-(3-bromophenyl)-5-phenyl- (II f) and 5-(3-bromophenyl)-2-(4-pyridyl)-1,3,4-oxadiazoles (IIIe) with the experimental values. For illustration, the chemical shifts of the 3-bromophenyl fragment in IIIe calculated using the increments (ppm) reported for monosubstituted benzenes [13] (for Br $\Delta\delta_i = -5.8$, $\Delta\delta_o = 3.2$, $\Delta\delta_m = 1.6$, and $\Delta\delta_p = -1.6$) and our data for the 1,3,4-oxadiazole substituent (see above) are compared with the experimental data:

TABLE 2. ¹³C NMR Spectra of 2-Ar-5-R-Substituted Oxadiazoles I-III

Com- pound	Chemical shifts, δ , ppm					
	Ar				R	Oxadi- azole C(2) C(5)
	C(1)	C(2)/C(6)	C(3)/ C(5)	C(4)		
1	2	3	4	5	6	7
Ia	Ph: 123,8	126,8	128,9	131,3	Me: 11,0	164,2, 164,9
Ib	2,4,5-Me ₃ C ₆ H ₄ : 120,3, 134,3/129,7, 133,0/135,4 2-, 4-, 5-Me: 19,1, 19,6, 21,3			140,0	Me: 11,0	162,8, 165,3
IIa	Ph: 123,7	126,7	128,9	131,5	Ph: 123,7, 126,7, 128,9, 131,5	164,3
IIb	Ph: 123,2	127,0	129,2	132,1	2-HOC ₆ H ₄ : 1'-C 108,1, 2'-C 157,7, 3'-C 117,6, 4'-C 133,7, 5'-C 119,9, 6'-C 126,5	164,2, 163,2
IIc	Ph: 123,3	127,1	129,1	132,1	2-O ₂ NC ₆ H ₄ : 1'-C 118,5, 2'-C 148,3, 3'-C 124,6, 4'-C 132,5, 5'-C 133,1, 6'-C 131,6	161,2, 165,7
IId	Ph: 123,4	127,1	129,3	132,3	3-O ₂ NC ₆ H ₄ : 1'-C 125,6, 2'-C 121,7, 3'-C 148,7, 4'-C 126,2, 5'-C 130,5, 6'-C 132,5	162,6, 165,3
IIe	Ph: 122,6	127,2	129,3	132,4	4-O ₂ NC ₆ H ₄ : 1'-C 129,5, 2'- и 6'-C 127,8, 3'-and5'-C 124,5, 4'-C 149,6	163,0, 165,7
IIf	Ph 123,6	127,0	129,1	131,9	3-BrC ₆ H ₄ : 1'-C 125,7, 2'-C 129,7, 3'-C 123,1, 4'-C 134,6, 5'-C 130,7, 6'-C 125,4	163,2, 165,0
IIg	Ph 124,0	126,7	128,9	131,4	2,4-Me ₂ C ₆ H ₃ : 1'-C 120,1, 2'-C 138,1, 3'-C 132,4, 4'-C 141,5, 5'-C 126,8, 6'-C 128,8, 2'-, 4'-Me: 21,9, 21,2	164,9, 163,7
IIh	Ph: 124,0	126,7	128,9	131,3	2,4,5-Me ₃ C ₆ H ₂ : 1'-C 120,2, 2'-C 134,3, 3'-C 133,0, 4'-C 140,2, 5'-C 135,4, 6'-C 129,6, 2'-, 4'-, 5'-Me: 19,0, 19,5, 21,4	165,0, 163,7
IIi	2,4-Me ₂ C ₆ H ₃ : 119,3 2-, 4-Me: 21,4, 22,2	138,4/ 128,8 21,4, 22,2	132,6/ 127,0	142,1	2-HOC ₆ H ₄ : 1'-C 108,1, 2'-C 157,6, 3'-C 117,5, 4'-C 133,4, 5'-C 119,8, 6'-C 126,5	163,4, 163,3
IIk	2,4- Me ₂ C ₆ H ₃ : 119,5 2-, 4-Me: 21,4, 22,1	138,5/129,0	132,7/ 127,1	142,2	3-O ₂ NC ₆ H ₄ : 1'-C 125,7, 2'-C 121,6, 3'-C 148,6, 4'-C 125,9, 5'-C 130,4, 6'-C 132,3	161,9, 165,6
IIl	2,4- Me ₂ C ₆ H ₃ : 119,7 2, 4-Me: 21,4, 22,1	138,7/129,2	132,9/ 127,2	142,5	4-O ₂ NC ₆ H ₄ : 1'-C 129,5, 2'-C 127,9, 3'-and 5'-C 124,5, 4'-C 149,5	162,3, 166,1
IIm	2,4,5- Me ₃ C ₆ H ₄ : 119,3 2-, 4-, 5- Me: 19,1, 19,6, 21,8	134,6/129,7	133,4/ 135,7	140,0	2-HOC ₆ H ₄ : 1'-C 108,1, 2'-C 157,5, 3'-C 117,4, 4'-C 133,5, 5'-C 119,8, 6'-C 126,4	163,5, 163,2

TABLE 2 (continued)

1	2	3	4	5	6	7
II o	2,4,5- Me ₃ C ₆ H ₄ : 119,8 2-, 4-, 5-Me:	134,9/ 129,9 19,1, 19,7, 21,5	133,3/ 135,9	141,0	3-O ₂ NC ₆ H ₄ : 1'-C 125,8, 2'-C 121,6, 3'-C 148,7, 4'-C 125,9,9, 5'-C 130,4, 6'-C 132,4	161,9 165,8
II p	2,4,5- Me ₃ C ₆ H ₄ : 119,8 2-, 4-, 5-Me:	134,9/ 130,1 19,3, 19,9, 21,6	133,5/ 136,1	141,3	4-O ₂ NC ₆ H ₄ : 1'-C 129,8, 2'- и 6'-C 127,9, 3'- и 5'-C 124,6, 4'-C 149,9	162,3, 165,1
II q	2,3,4,5-Me ₄ C ₆ H ₁ : 120,1 2-,3-,4-, 5-Me:	134,4/ 128,1 16,6, 16,7, 17,9, 20,8	137,1 134,4	139,6	3-O ₂ NC ₆ H ₄ : 1'-C 125,9, 2'-C 121,7, 3'-C 148,7, 4'-C 126,0, 5'-C 130,4, 6'-C 132,5	162,2, 166,5
II r	2,3,4,5-Me ₄ C ₆ H ₁ : 119,8 2-, 3-, 4-, 5-Me:	134,3/ 127,9 16,4, 16,6, 17,8, 20,7	136,9/ 134,3	139,5	2-HOC ₆ H ₄ : 1'-C 108,2, 2'-C 157,6, 3'-C 117,5, 4'-C 133,4, 5'-C 119,8, 6'-C 126,5	164,2, 163,5
III a	Ph: 123,1	127,2	129,2	132,3	4,5-Br ₂ -2-C ₄ H ₁₀ : 2'-C 127,5, 3'-C 118,2, 4'-C 104,4, 5'-C 141,3	164,4, 155,8
III b	Ph: 123,6	126,8	129,0	131,7	2-C ₄ H ₃ S: 2'-C 125,1, 3'-C 129,7, 4'-C 128,1, 5'-C 130,1	163,9, 160,7
III e	Ph: 123,3	126,9	129,1	132,0	3-C ₅ H ₄ N: 2'-C 147,7, 3'-C 120,3, 4'-C 134,0, 5'-C 123,7, 6'-C 152,3	164,9, 162,4
III d	Ph: 123,2	127,0	129,1	132,1	4-C ₅ H ₄ N: α -C 150,8, β-C 120,1, γ-C 130,8	165,3, 162,6
III e	3-BrC ₆ H ₄ : 125,1	129,8/ 125,6	123,2/ 130,7	135,1	4-C ₅ H ₄ N: α -C 150,9, β-C 120,2, γ-C 132,5	164,0, 163,0
III h	2,4-Me ₂ C ₆ H ₃ : 119,5 2- и 4-Me:	138,2/128,7 21,2, 21,9	132,4/ 126,8	141,8	3-C ₅ H ₄ N: 2'-C 147,6, 3'- 120,3, 4'-C 133,7, 5'-C 123,6, 6'-C 152,0	165,1, 161,5
III j	2,4-Me ₂ O ₆ H ₃ : 119,5 2- и 4-Me:	138,5/129,0 21,4, 22,0	132,6/ 127,0	142,2	4-C ₅ H ₄ N: α -C 150,8, β-C 120,2, γ-C 131,1	165,8, 162,0
III l	2,4,5-Me ₃ C ₆ H ₄ : 119,6 2-, 4-, 5-Me:	134,3/129,5 18,9, 19,4, 21,3	133,0/ 135,4	140,4	3-C ₅ H ₄ N: 2'-C 147,5, 3'-C 120,3, 4'-C 133,7, 5'-C 123,5, 6'-C 151,9	165,2, 161,4
III m	2,4,5-Me ₃ C ₆ H ₄ : 119,6 2-, 4-, 5-Me:	134,5/129,7 19,0, 19,6, 21,4	133,1/ 135,7	140,8	4-C ₅ H ₄ N: α -C 150,7, β-C 120,1, γ-C 131,0	165,8, 161,9

*C₍₂₎.*2C₍₅₎.

$$\begin{aligned} \delta C_{(1)} &= 128.5 + 1.6 - 4.8 = 125.3 \text{ (exp } \delta C_{(1)} = 125.1 \text{ ppm)} \\ \delta C_{(2)} &= 128.5 + 3.2 - 1.8 = 129.9 \text{ (exp } \delta C_{(2)} = 129.8 \text{ ppm)} \\ \delta C_{(3)} &= 128.5 - 5.8 + 0.4 = 123.1 \text{ (exp } \delta C_{(3)} = 123.2 \text{ ppm)} \\ \delta C_{(4)} &= 128.5 + 3.2 + 3.0 = 134.7 \text{ (exp } \delta C_{(4)} = 135.1 \text{ ppm)} \\ \delta C_{(5)} &= 128.5 + 1.6 + 0.4 = 130.5 \text{ (exp } \delta C_{(5)} = 130.7 \text{ ppm)} \\ \delta C_{(6)} &= 128.5 - 1.6 - 1.8 = 125.1 \text{ (exp } \delta C_{(6)} = 125.6 \text{ ppm)} \end{aligned}$$

The best agreement with the experimental data was obtained in calculating the chemical shifts for pyridine and also mono- and disubstituted benzene rings (with the exception of the 2-hydroxyphenyl fragment). The results of the calculations for 2,4-dimethylphenyl, 2,4,5-trimethylphenyl, and 2,3,4,5-tetramethylphenyl fragments do not always unequivocally correspond to the experimental data. In these cases, the assignment of the signals was carried out using heteronuclear double resonance and indirectly supported by comparing our results with literature data [2-6, 8]. Thus, the ^{13}C NMR spectrum of 2,5-diphenyl-1,3,4-oxadiazole (IIa) fully corresponds to the spectrum given by Tashtoush [8], while the spectra of 2-(2,4-dimethylphenyl)-5-phenyl-1,3,4-oxadiazole (IIg) and its 2,4,5-trimethylphenyl homolog (II) are in good accord with the spectra of 2-(2,4,6-trimethylphenyl)-5-phenyl-1,3,4-oxadiazole and 2,5-bis(2,4,6-trimethylphenyl)-1,3,4-oxadiazole [5].

Considerable difficulties arise in assigning the ^{13}C NMR signals of the oxadiazole ring, which, as a rule, differ only slightly among each other. Such assignments were carried out only for IIIa and IIIb taking account of the reported data reported for symmetrical 2,5-di(2-furyl)- and 2,5-di(2-thienyl)-1,3,4-oxadiazoles [8].

Our results permit a quantitative evaluation of the effect of 5-R-1,3,4-oxadiazol-2-yl fragments as benzene ring substituents using the well-known linear correlation between electrophilic substituent constants σ_p^+ and the chemical shifts of the para carbon atoms in monosubstituted benzenes [14]. Since the data of Nelson et al. [14] were obtained for chemical shifts in CCl_4 and for relatively limited data (11 compounds), we used the $\Delta\delta_p$ values for 28 monosubstituted benzenes in CDCl_3 from the review of Ewing [13], which were compared with σ_p^+ constants of the corresponding substituents taken from the work of Swain and Lupton [15] (the lacking value for the CHO group was taken from the monograph of Levy and Nelson [16]). The linear correlation obtained using the method of least squares (the correlation coefficient was 0.960) permits facile determination of σ_p^+ constants using the data in Table 2 and the following analytical expression:

$$\sigma_p^+ = \frac{\Delta\delta_p + 1.08}{8.51} \quad (3)$$

The σ_p^+ values for the substituents studied vary in a rather narrow range: from 0.45 for 5-(2,4,5-trimethylphenyl)-1,3,4-oxadiazol-2-yl (IIh) to 0.57 for IIc (R = 3-nitrophenyl) and IIId (R = 4-pyridyl). The values of σ_p^+ of such substituents as 5-cyano-1,3,4-oxadiazol-2-yl (0.67), 5-methoxy-1,3,4-oxadiazol-2-yl (0.43), and 5-methylthio-1,3,4-oxadiazol-2-yl (0.42) calculated using literature data [2, 3] lie beyond this range. These values support the above observation that the oxadiazolyl fragment in I-III serves to "level out" the effect of a substituent at $C_{(5)}$ on the phenyl group at $C_{(2)}$. The transmission capacity of the oxadiazolyl ring may be evaluated by comparing the chemical shift data $\Delta\delta_{C_p}$ for 5-R-2-phenyl-1,3,4-oxadiazoles (Ia, IIa, IIb, IIc-IIf, and IIb-IIId from the present work and 5-methoxy-, 5-methylthio-, and 5-cyano-1,3,4-oxadiazoles from the work of Aranda [2] and Terui [3]) with the $\Delta\delta_{C_p}$ values of the corresponding R-substituted benzenes, which were taken from the review of Ewing [13] (for R = Me, Me, MeS, CN, and Ph) and other workers: R = 2-thienyl [17], R = 3-pyridyl and 4-pyridyl [18], R = 3- BrC_6H_4 [19], R = 3- $\text{O}_2\text{NC}_6\text{H}_4$ [20], R = 4- $\text{O}_2\text{NC}_6\text{H}_4$ [21], and R = 2- HOC_6H_4 [22]. The corresponding points lie rather satisfactorily on a line ($r = 0.973$) described by the following equation:

$$\Delta\delta_{C_p}(\text{OD}) = 0,30 \cdot \Delta\delta_{C_p}(\text{PhX}) + 3,58 \quad (4)$$

The slope of this line shows that the substituent effect in transmission through the oxadiazole ring is diminished by a factor of ~ 3 while the free term corresponds to $\Delta\delta_{C_p}$ of 2-phenyl-1,3,4-oxadiazole (R = H) and is 3.58 ppm. This value permits us to use Eq. (3) to find σ_p^+ of the 1,3,4-oxadiazol-2-yl fragment as 0.55, which is significantly more than for 2-oxazolonyl (0.33) [22] and, even more so, for 2-furyl (-0.02), which we calculated using the ^{13}C NMR data for 2-phenyl-furan from the review of Ewing [13]. These estimates indicate that when the CH fragment in the furan ring is replaced by a "pyridinic" nitrogen atom, the substituent is converted into electron-withdrawing and the electron-withdrawing capacity becomes even greater when the second fragment is replaced.

In regard to the decrease in the substituent effect upon transmission through the oxadiazole ring, the value indicated is not evidence for low transmission capacity of this ring. Our treatment of the data of 14 diphenyl derivatives and 14 corresponding monosubstituted benzenes [21] led to a linear correlation ($r = 0.968$).

$$\Delta\delta C_p (\text{Ph—Ar}) = 0,15 \cdot \Delta\delta C_p (\text{PhX}) + 0,57 \quad (5)$$

Equation (5) shows that the substituent effect in diphenyl derivatives is less than half than upon transmission through the oxadiazole fragment. According to electron diffraction data [24], the noncoplanarity of the diphenyl system is characterized by virtually the same parameters as for 2,5-diphenyl-1,3,4-oxadiazole: the dihedral angle between the two benzene rings for diphenyl and a number of its derivatives with free ortho positions is close to 45° .

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra for I-III were taken in the pulse mode with Fourier transformation on a Bruker WM-250 spectrometer at 250 MHz for the ^1H NMR spectra and Bruker AM-300 spectrometer at 300 MHz for ^{13}C NMR and 75.5 MHz for ^{13}C NMR spectra. CDCl_3 was used as the solvent (δ 7.27 ppm for the ^1H NMR spectra and δ 77.1 ppm for the ^{13}C NMR spectra). The resonance conditions were stabilized relative to the ^2H signals of the solvent. The computer memory capacity was 16K. The pulse length was 3 μsec (45°) for measurements of the ^{13}C NMR spectra and 1 μsec (15°) for the ^1H NMR spectra. The difference between the signals of the CH_3 , CH_2 , and C_{quat} carbons were obtained using the standard JMOD HX.AO program for spectral editing. Heteronuclear double resonance was used for assigning the signals in the ^{13}C NMR spectra of IIc, IIr, IIIa, IIIb, IIIh, and IIIm.

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