Reference Data

No clear relationship between shielding tensor parameters and structural type emerged from this study, although this may be a result of inadequate crystallographic data.

EXPERIMENTAL

All the metal acetates were commercially available with the exception of barium acetate monohydrate. This was prepared by reaction of excess of barium carbonate and aqueous acetic acid, with stirring, for several hours. Crystals were obtained by filtering and evaporating the solution. The samples were packed as crystalline powders into standard double-bearing rotors of outside diameter 7 mm. The high-resolution ^{13}C NMR spectra were obtained using a Bruker CXP 200 spectrometer operating at 50.323 MHz under conditions of cross polarization, magic-angle spinning (CP/MAS) and high-power proton decoupling at ambient probe temperature (*ca* 30 °C).

Depending on the sample, the contact time used varied between 2 and 10 ms, and a typical value of the recycle delay was 5 s. The number of transients varied from a few hundred to 8000 to obtain reasonable signal-to-noise ratios. The spectra were recorded with a typical spectral width of 20 kHz using 4K data points, the final 2K of which were zeroed before Fourier transformation. The computer program used iteratively to fit the spinning sideband manifolds was written by Ascenso *et al.*[19]

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^{1}H and ^{13}C NMR Spectroscopy of Substituted Bis-1,3,4-oxadiazoles

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Dehydration of *N,N'*-diacylalkanedioic acid dihydrazides with phosphoryl chloride gave 5,5'-disubstituted-2,2'-(1,*n*-alkanediyl)bis-1,3,4-oxadiazoles. The structures of these compounds were elucidated by ^{1}H, ^{13}C NMR, UV and IR spectroscopy.

KEY WORDS Bis-1,3,4-oxadiazoles ^{1}H NMR ^{13}C NMR

INTRODUCTION

The most extensively studied oxadiazoles are the 1,3,4-isomers, which are of significance in industrial and biological applications,[1-4] but little attention has been paid to substituted bis-1,3,4-oxadiazoles.[5,6] In a preliminary report[7] we demonstrated that Stolle's method[8] for the preparation of 1,3,4-oxadiazoles can be extended to the synthesis of alkyl- and aryl-substituted bis-1,3,4-oxadiazoles. Among the numerous dehydration reagents used,[9-11] we found that a mixture of phosphoryl chloride and acetonitrile (1:8) gave the best results. In connection with this project, a series of 5,5'-disubstituted-2,2'-(1,*n*-alkanediyl)bis-1,3,4-oxadiazoles (**2a–z**) were prepared by the dehydration of the corresponding substituted alkanedioic acid dihydrazides **1** (n = 0, 1, 3, 4, 8) (Table 1). The structures of compounds **2a–z** were elucidated by ^{1}H, ^{13}C NMR, UV and IR spectroscopy.

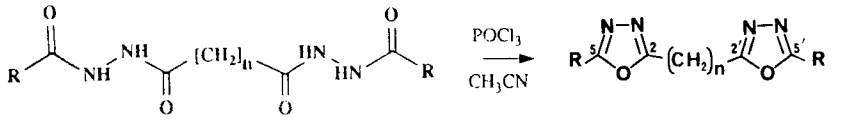
RESULTS AND DISCUSSION

The IR spectra of compounds **2** with R = alkyl display strong to moderate absorptions in the 1640–1560 cm^{-1} range, assigned to the C=N bonds of the oxadiazole moieties. When R = aryl, an additional absorption was observed in the range 1520–1490 cm^{-1}. ^{1}H and ^{13}C NMR spectra were in full agreement with the assigned structures. Tables 2 and 3 summarize the ^{1}H NMR, UV and ^{13}C NMR data for **2a–z**. The ^{13}C NMR spectra exhibit characteristic signals for C-2 of the oxadiazole ring at δ 164.3–166.9 ppm, whereas the C-5 signals absorb at δ 156.5–172.9 ppm and show a strong dependence on the nature of the R substituent. When R = 2-furyl or 2-thienyl, the C-5 resonance appears between δ 156.5 and 159.0 ppm. For R = phenyl or substituted phenyl the C-5 signal is at δ 161.2–165.9 ppm, and for R = alkyl C-5 resonates at δ 166.1–172.5 ppm. Alkyl-substituted bis-1,3,4-oxadiazoles exhibit UV absorptions (methanol) in the range λ_{max} = 193–229 nm (log ε = 4.3–4.9).

EXPERIMENTAL

Melting points were measured on an electrothermal digital melting point apparatus. The ^{13}C NMR spectra were recorded in the PFT mode at ambient temperature with internal deuterium lock using a Bruker WP 80-SY spectrometer (20 MHz). The pulse duration was 3 μs and the sweep width was 4500 Hz. The ^{1}H NMR spectra were recorded on a Bruker WP 80-SY spectrometer (80 MHz).

Table 1. Structures, yields and melting points of substituted bis-1,3,4-oxadiazoles



1a–z 2a–z

Compound 1, 2[a]	n	R	Yield (%)	M.p. (°C)
a	0	C_6H_5	88	138–139
b	0	4-$MeOC_6H_4$	89	203–204
c	0	4-$O_2NC_6H_4$	82	234–235
d	0	4-FC_6H_4	86	207–208
e	1	4-$O_2NC_6H_4$	80	193–194
f	1	4-FC_6H_4	83	188–189
g	1	2-Furyl	86	126–127
h	1	2-Thienyl	82	133–134
i	1	CH_3	77	110–111
j	3	4-$MeOC_6H_4$	89	175–176
k	3	4-$O_2NC_6H_4$	79	198–199
l	3	4-FC_6H_4	87	168–169
m	3	2-Thienyl	84	145–146
n	3	$(CH_3)_2CH$	78	117–118
o	4	4-$MeOC_6H_4$	94	191–192
p	4	4-$O_2NC_6H_4$	84	215–216
q	4	4-FC_6H_4	84	170–171
r	4	CH_3	80	107–108
s	4	$(CH_3)_2CH$	81	111–112
t	4	$(CH_3)_3C$	81	118–119
u	8	C_6H_5	92	173–174
v	8	4-$MeOC_6H_4$	95	180–181
w	8	4-$O_2NC_6H_4$	82	195–196
x	8	4-FC_6H_4	88	138–139
y	8	$(CH_3)_2CH$	85	98–99
z	8	$(CH_3)_3C$	80	84–85

[a] Names of selected compounds: **2a** = 5,5′-diphenyl-2,2′-bis-1,3,4-oxadiazole; **2g** = 5,5′-di(2-furyl)-2,2′-(methanediyl)bis-1,3,4-oxadiazole; **2n** = 5,5′diisopropyl-2,2′-(propane-1,3-diyl)bis-1,3,4-oxadiazole; **2p** = 5,5′-di(*p*-nitrophenyl)-2,2′-(butane-1,4-diyl)bis-1,3,4-oxadiazole; **2z** = 5,5′-di(*tert*-butyl)-2,2′-(octane-1,8-diyl)bis-1,3,4-oxadiazole.

Table 2. UV and ^{1}H NMR data for compounds 2a–z

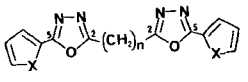
Compound 2[a]	UV (CH_3OH): λ_{max} (nm) with log ε in parentheses	^{1}H NMR ($CDCl_3$–TMS)[b,c]: δ (ppm)
a	266 (4.7), 203 (4.7)	7.93 (m, Ph), 7.50 (m, Ph)
b	280 (4.8), 212 (4.7)	7.99 (m, 4H, Ph), 7.10 (m, 4H, Ph), 3.86 (s, 6H, OCH_3)
c	290 (4.8), 228 (4.6)	8.28 (m, Ph)
d	260 (4.9), 204 (4.9)	8.16 (m, 4H, Ph), 7.18 (m, 4H, Ph)
e	285 (4.9), 229 (4.5)	8.14 (m, 8H, Ph), 4.88 (s, 2H, CH_2)
f	251 (4.8), 201 (4.9)	8.05 (m, 4H, Ph), 7.19 (m, 4H, Ph), 4.67 (s, 2H, CH_2)
g	265 (4.7)	7.64 (m, 2H), 7.12 (m, 2H), 6.57 (m, 2H) (furyl), 4.84 (s, 2H, CH_2)
h	283 (4.8), 260 (4.7)	7.73 (m, 2H), 7.55 (m, 2H), 7.13 (m, 2H) (thienyl), 4.63 (s, 2H, CH_2)
i	196 (4.7)	4.68 (s, 2H, CH_2), 2.53 (s, 6H, CH_3)
j	269 (4.9), 208 (4.8)	7.93 (m, 4H, Ph), 7.00 (m, 4H, Ph), 3.86 (s, 6H, OCH_3), 3.11 (t, 4H, J = 7.3 Hz, CH_2), 2.48 (q, 2H, J = 7.3 Hz, CH_2)
k	285 (4.8), 223 (4.5)	8.16 (m, 8H, Ph), 3.13 (t, 4H, J = 7.1 Hz, CH_2), 2.44 (q, 2H, J = 7.1 Hz, CH_2)
l	249 (4.8), 201 (4.9)	8.00 (m, 4H, Ph), 7.20 (m, 4H, Ph), 3.14 (t, 4H, J = 7.0 Hz, CH_2), 2.5 (q, 2H, J = 7.0 Hz, CH_2)
m	282 (4.8), 260 (4.7)	7.74 (m, 2H), 7.55 (m, 2H), 7.20 (m, 2H) (thienyl), 3.11 (t, 4H, J = 7.2 Hz, CH_2), 2.48 (q, 2H, J = 7.2 Hz, CH_2)
n	203 (4.3)	3.23 (h, 2H, J = 6.7 Hz, CH_2), 3.06 (t, 4H, J = 7.1 Hz, CH_2), 2.43 (q, 4H, J = 7.1 Hz, CH), 1.34 (d, 12H, J = 6.7 Hz, CH_3)

Table 2—continued

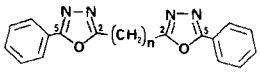
Compound	UV (CH_3OH): λ_{max} (nm) with log ε in parentheses	^1H NMR ($CDCl_3$–TMS)[b,c]: δ (ppm)
o	269 (4.8), 223 (4.5)	7.94 (m, 4H, Ph), 6.96 (m, 4H, Ph), 3.85 (s, 6H, OCH_3) 2.94 (m, 4H, CH_2), 2.00 (m, 4H, CH_2)
p	285 (4.8), 223 (4.5)	8.25 (m, 8H, Ph), 3.08 (m, 4H, CH_2), 2.09 (m, 4H, CH_2)
q	250 (4.9), 203 (4.5)	8.00 (m, 4H, Ph), 7.14 (m, 4H, Ph), 2.90 (m, 4H, CH_2), 1.95 (m, 4H, CH_2)
r	196 (4.7)	2.98 (m, 4H, CH_2), 2.56 (s, 6H, CH_3), 2.04 (m, 4H, CH_2)
s	202 (4.7)	3.16 (h, 2H, J = 6.9 Hz, CH), 2.95 (m, 4H, CH_2), 2.03 (m, 4H, CH_2), 1.35 (d, 12H, J = 6.9 Hz, CH_3)
t	198 (4.7)	3.04 (m, 4H, CH_2), 2.05 (m, 4H, CH_2), 1.43 (s, 18H, CH_3)
u	250 (4.6), 203 (4.8)	8.03 (m, 4H, Ph), 7.43 (m, 6H, Ph), 2.93 (t, 4H, J = 7.5 Hz, CH_2), 1.84 (m, 4H, CH_2), 1.41 (m, 8H, CH_2)
v	269 (4.9), 223 (4.6)	7.95 (m, 4H, Ph), 7.02 (m, 4H, Ph), 3.86 (s, 6H, OCH_3), 2.90 (t, 4H, J = 7.2 Hz, CH_2), 1.83 (m, 4H, CH_2), 1.40 (m, 8H, CH_2)
w	286 (4.9), 223 (4.6)	8.20 (m, 8H, Ph), 2.98 (t, 4H, J = 7.2 Hz, CH_2), 1.79 (m, 4H, CH_2), 1.39 (m, 8H, CH_2)
x	250 (4.9)	8.06 (m, 4H, Ph), 7.21 (m, 4H, Ph), 2.98 (t, 4H, J = 7.6 Hz, CH_2), 1.80 (m, 4H, CH_2), 1.44 (m, 8H, CH_2)
y	202 (4.3)	3.12 (h, 2H, J = 6.9 Hz, CH), 2.79 (t, 4H, J = 7.6 Hz, CH_2), 1.75 (m, 4H, CH_2), 1.36 (d, 12H, J = 6.9 Hz, CH_3), 1.31 (m, 8H, CH_2)
z	198 (4.7)	2.82 (t, 4H, J = 7.7 Hz, CH_2), 1.72 (m, 4H, CH_2), 1.41 (s, 18H, CH_3), 1.36 (m, 8H, CH_2)

[a] Satisfactory microanalyses were obtained for all the compounds.
[b] All spectra were recorded at 302 K.
[c] q = Quintet; h = septet.

Table 3. ^{13}C NMR data for compounds 2a–z ($CDCl_3$–TMS)



X: O, S



Compound 2	C-2	C-5	Aromatic carbons C-a	C-b	C-c	C-d	Methylene carbons	Other carbons
a	166.5	165.3	131.6	129.0	126.7	132.2		
b	166.1	164.5	129.1	115.4	114.8	159.8		55.4 (OCH_3)
c	166.3	165.7	127.0	126.3	124.5	123.3		
d	165.8	164.8	128.9	116.9	115.8	130.0[a]		
e	164.8	161.2	128.1	127.2	123.9	128.1[a]	22.8	
f	164.6	160.9	128.5	116.9	116.0	129.2[a]	23.0	
g	165.1	156.5	146.1	113.9	112.4	138.4	22.9	
h	165.2	158.5	137.8	129.4	125.5	128.3	23.1	
i	164.9	166.1					22.7	10.4 (CH_3)
j	165.1	164.8	128.5	116.6	114.5	162.4	24.6, 23.2	55.4 (OCH_3)
k	165.6	164.6	127.5	124.1	123.6	128.3[a]	24.5, 23.5	
l	165.3	164.1	128.8	116.3	115.1	130.0[a]	24.5, 23.3	
m	165.1	159.1	138.4	129.2	125.4	128.2	24.5, 23.3	
n	165.7	170.7					24.4, 23.4	32.2 (CH), 21.4 (CH_3)
o	165.6	164.7	123.5	116.7	114.5	162.3	25.7, 24.9	55.3 (OCH_3)
p	166.2	163.6	127.5	124.2	123.2	128.6[a]	24.9, 23.9	
q	166.3	163.5	128.9	116.6	115.8	129.2[a]	24.9, 23.7	
r	164.9	169.3					25.4, 24.3	10.2 (CH_3)
s	166.8	169.9					26.3, 24.4	29.1 (CH), 28.6 (CH_3)
t	165.4	172.5					26.2, 24.5	32.0 (C), 28.6 (CH_3)
u	166.9	165.1	131.5	125.8	123.5	129.2	29.1, 26.4, 25.6	
v	166.6	164.8	123.3	117.0	114.5	160.2	29.6, 26.3, 25.3	55.4 (OCH_3)
w	166.3	165.9	127.8	124.0	123.2	128.7[a]	29.5, 26.5, 25.4	
x	166.9	163.9	128.8	116.8	115.7	129.3[a]	28.9, 26.5, 25.4	
y	164.3	171.4					28.1, 26.5, 25.3	29.6 (CH), 21.8 (CH_3)
z	165.6	171.7					28.7, 26.4, 25.3	32.3 (C), 27.0 (CH_3)

[a] Ambiguous assignments.

Reference Data

The pulse duration was 1 μs and the sweep width was 800–1050 Hz. All chemical shifts were determined on the δ scale (ppm) relative to internal tetramethylsilane. UV spectra were recorded in methanol on a Cary 2390 spectrophotometer linked to a DS-15 data station with an Epson LX-80 recorder. IR spectra were recorded on a Pye Unicam SP 300 spectrophotometer as potassium bromide pellets. *N,N'*-Diacylalkanedioic acid dihydrazides were prepared as described previously.[12]

Preparation of bis-1,3,4-oxadiazoles 2a–z

A mixture of the appropriate *N,N'*-diacylalkanedioic acid dihydrazide **1** (7.5 mmol) and phosphoryl chloride (5 ml) in acetonitrile (40 ml) was boiled under reflux for 2 h. The reaction mixture was concentrated to a volume of about 20 ml and poured into 100 ml of ice–water. The product was normally filtered off, washed with water, dried over magnesium sulphate and recrystallized from chloroform–hexane (2:3). However, in the case of alkyl-substituted bis-1,3,4-oxdiazoles, the product was quickly extracted with chloroform (4 × 50 ml) at 0 °C, otherwise most of the product hydrolysed and the yield was reduced. The combined extracts were dried over magnesium sulphate, filtered and the soivent was removed under reduced pressure. The residue was recrystallized from chloroform–hexane (2:3).

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Book Review

E. BUNCEL and J. R. JONES (Eds)
Isotopes in the Physical and Biomedical Sciences. Vol. 1, Labelled Compounds (Part B)

Elsevier, Amsterdam, 1991, pp. 444, US $215. ISBN 0 444 89186 2.

The Editors say in their Preface to this series that they intend to survey advances in the synthesis and applications of isotopically labelled compounds by commissioning active scientists to review specific areas. A specific introduction to this volume, explaining its purpose and function, is not provided. The ten areas (Chapters) are: Radiolabelled insecticides, herbicides and fungicides; Isotopically labelled histamine H_2-receptor antagonists; Preparation of tritium-labelled steroids; Synthesis and applications of tritiated affinity probes; Tritium-labelled hormones, pheromones and odorants; Labelled eicosanoids; Isotopically labelled gibberellins; Preparation of radiohalogenated biomolecules via organotin intermediates; Use of enzymes in the synthesis of stereospecifically labelled compounds; and Protein labelling agents.

These mongraphs have been reproduced directly from the contributors' typescripts, with the variety of typographic styles and absence of cross-references that are to be expected from 'camera-ready' copy. The Editors do not appear to have attempted to impose a uniform style on the contributors, which has resulted in references and labelling sites being quoted according to different conventions, and in half of the contributions molecules are labelled whereas in the remainder they are labeled! Occasional lines of text are to be found inserted at single spacing between otherwise double-spaced articles. In contrast to this evidence of overhasty preparation, the quality of the printing, paper and binding is superb.

The emphasis is on the preparation of labelled compounds, although the depth of treatment is very variable. They range from a compilation of preparations of labelled eicosanoids, replete with full preparative experimental details—which results in an article to refer to rather than to read—to general surveys containing statements such as, 'aniline is substituted with radioiodine using a chloramine-T-mediated oxidative methods,' together with the literature reference.

The applications sections are concise and informative, but concentrate largely on radio tracer studies of metabolism, degradation and function. The extensive use of labelled compounds in the study of molecular structure and dynamics does not appear. NMR is only briefly mentioned and then only as a means of confirming the site of the label. Very little reference is made to other molecular spectroscopic data.

Overall, this book is unlikely to be of interest to the general spectroscopic community; only those who wish to prepare isotopically labelled compounds for themselves may find it useful. Those wishing to synthesize a particular labelled compound will probably find direct access to the primary literature via computer search more convenient.

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