Synthesis and ^1H Nuclear Magnetic Resonance Spectra of Some Aryl-1,2,3-selenadiazoles

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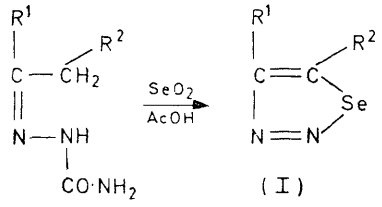
A series of aryl-1,2,3-selenadiazoles has been prepared, and their n.m.r. spectral parameters are recorded. The ranges of chemical shifts of the 5-proton due to *meta*- or *para*-substitution in the 4-aryl substituent are similar to those for the corresponding protons in the side-chains of substituted benzenes.

THE synthesis of the 1,2,3-selenadiazole system has recently been reported.[1] We have synthesised a number of crystalline, well-defined compounds containing this ring system for biological evaluation, and we report here the major physical properties of these compounds, of general formula (I), where R^1 is an aromatic group, generally benzenoid in nature, and R^2 is generally H (see Table). The synthetic reaction proved to be quite general,[1c] high yields of the single, desired product being obtained in most cases.† In some cases, difficulties were encountered, and the experimental conditions were modified slightly to obtain optimum yields (see Experimental section).



(I)

The reactions of the semicarbazones of aminoaryl ketones gave a mixture of unidentified products, owing to the sensitivity of the amino-group.[2] None of the desired product was obtained by any alteration of the reaction conditions. The hydroxy-derivatives (7) and (13) were obtained directly by alkaline hydrolysis of the appropriate acetoxy-derivatives. The reaction proceeded smoothly with the semicarbazone of 2-acetylnaphthalene, but none of the desired product was obtained with that of 1-acetylnaphthalene.

Quaternisation of the pyridyl derivatives (25)—(27) was attempted. No pure products were isolated from the reaction with methyl bromide, but pure, crystalline methiodide was obtained with methyl iodide in the case of the 3-pyridyl derivative (26). The product was identified by elemental analysis and n.m.r. data, the pyridine ring protons showing the usual shifts associated with quaternisation.[3]

^1H N.m.r. Spectra.—For each compound where R^2 = H, the H-5 signal appears as a single, sharp peak, except for the case of the *ortho*-fluoro-derivative (17), where a doublet, arising from coupling with the *ortho*-fluorine nucleus, was noted (J 0·9 Hz; *cf.* the acetylenic proton in *o*-fluorophenylacetylene, J 0·8 Hz.[4]). No coupling was observed for the *para*-fluoro-derivative (2), in contrast to that observed for the acetylenic proton in *p*-fluorophenylacetylene (J 0·8 Hz, identical with that for the *ortho*-compound [4]).

For compounds (1)—(18), the chemical shift of H-5 can be likened to that of the corresponding proton in the side-chain of a substituted benzene.[3] Many authors have successfully correlated chemical shifts of side-chain protons with Hammett reactivity constants,[5] and we will report elsewhere the results of a comprehensive study of the chemical shifts in this system. However, a few general conclusions may be drawn here. Where comparisons are possible, the ranges of values for the *meta*- and *para*-substituted compounds (relative to the unsubstituted compound) are closely similar to those for the corresponding protons in phenylacetylenes,[4] styrenes,[5] stilbenes,[5,6] benzylideneacetones,[5] and benzylideneacetophenones.[5] No such parallel is observed, however, between the shifts for the *ortho*-derivatives (17) and (18), and those for the corresponding acetylenes.[4] In fact, the high-field shift of 0·27 p.p.m. observed for the *ortho*-nitro-derivative (18) relative to the *para*-nitro-derivative (9), can be compared with the similar shift to high-field (0·14 p.p.m.) observed for the methyl protons in the corresponding substituted acetophenones.[7]

EXPERIMENTAL

Analytical and u.v., i.r., and mass spectral data are available in Supplementary Publication No. SUP 20852 (12 pp., 1 microfiche).‡

M.p.s were determined with a Fisher–Johns hot-stage apparatus. ^1H N.m.r. spectra were determined with a JEOL MH-100 (100 MHz) spectrometer at ambient probe temperature (*ca.* 25°) for solutions in deuteriochloroform (tetramethylsilane as internal standard). T.l.c. plates were prepared from Kieselgel G (Merck); preparative plates were 1 mm thick. Chromatograms were developed with methanol–chloroform (1 : 19 v/v), and were examined under u.v. light. Evaporations were carried out at water-pump

† The synthesis of several of these compounds has previously been reported,[1b] though spectral parameters were not given. In one case ($R^1 = R^2$ = Ph), it was reported that the only product obtained under normal reaction conditions was the derived acetylene, but in our hands the reaction proceeded normally.

‡ For details of Supplementary Publications, see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20.

[1] I. Lalezari, A. Shafiee, and M. Yalpani, (*a*) *Tetrahedron Letters*, 1969, 5105; (*b*) *Angew. Chem.*, 1970, **82**, 484; (*c*) *J. Org. Chem.*, 1971, **36**, 2836.

[2] B. C. Challis and R. A. Butler, in 'The Chemistry of the Amino Group,' ed. S. Patai, Interscience, London, 1968, p. 320.

[3] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectrsocopy in Organic Chemistry,' 2nd edn., Pergamon, London, 1969, (*a*) p. 208; (*b*) p. 201; (*c*) p. 66.

[4] C. D. Cook and S. S. Danyluk, *Tetrahedron*, 1963, **19**, 177.

[5] J. P. Doucet, B. Ancian, and J. E. Dubois, *J. Chim. Phys.*, 1972, **69**, 188.

[6] H. Gusten and M. Salzwedel, *Tetrahedron*, 1967, **23**, 173.

[7] J. Bloxsidge, J. R. Jones, and R. E. Marks, *Org. Magnetic Resonance*, 1970, **2**, 337.

pressure at temperatures not exceeding 60°. All organic extracts were dried over anhydrous $MgSO_4$.

The ketones were all commercially available, and their purity was checked by m.p. or b.p. The semicarbazones were all prepared by conventional means, and were purified by crystallisation, usually from aqueous ethanol.

General Procedure for Preparation of Selenadiazoles (I).—The appropriate semicarbazone (0·01 mol) was added to glacial acetic acid (10 ml), and the mixture was stirred vigorously. The semicarbazone usually went into solution. Selenium dioxide (0·012 mol) was finely ground and added slowly. The temperature was then raised to 55—60°, and stirring and warming were continued for 1 h, or until t.l.c. indicated that the reaction was complete. The R_F value of the product was always considerably higher than that of the starting material. The mixture was then filtered hot under reduced pressure, the filtrate was allowed to cool to room temperature (still under reduced pressure), and the resulting precipitate was collected and washed with methanol. Otherwise, the product was obtained by quenching with water. The products were generally pure by t.l.c.; the yields reported in the Table are mostly those recorded at this stage. Compounds (18)—(20) and (24), were only obtained pure after crystallisation; the yields at this stage are recorded in the Table. For compound (11), elevated temperature (75—80°) and a slight excess of acetic acid were required to effect reaction.

Compounds (7) and (13) were prepared directly from the acetoxy-compounds (8) and (14) by alkaline hydrolysis. The acetoxy-compound (0·2 g) was dissolved in methanol (10 ml) by warming, and saturated sodium hydrogen carbonate solution was added slowly until precipitation occurred. The mixture was then stirred and warmed at 50° for 3 h; t.l.c. then indicated that the reaction was complete. The precipitate was filtered off, and the solution was concentrated to small volume; the product (pure by t.l.c.) precipitated.

The pyridyl compounds (25)—(27) were prepared by a modification of the general procedure. Prolonged reaction times were essential, and the reaction was best carried out by warming and stirring for 24 h, adding small quantities of selenium dioxide from time to time. The solution was then filtered under reduced pressure, and concentrated to small volume. Methanol was then added, and the solution was boiled with charcoal, filtered several times through Celite, and finally concentrated to small volume. The sticky semi-solid which separated was purified by preparative t.l.c., to give crystalline material.

Compound (26) was quaternised with methyl iodide in chloroform to give the *methiodide* (36%), m.p. 190—192° (from aqueous ethanol) (Found: C, 27·1; H, 2·3; N, 12·0. $C_8H_8IN_3Se$ requires C, 27·3; H, 2·3; N, 11·9%), δ[$(CD_3)_2$-SO] 10·58 (s, 5-H).

Physical data for the selenadiazoles (I)

Compound	R^1	R^2	Yield (%)	M.p.[a] (°C)	Solvent[b]	δ R^2[c]	δ Other[d]
(1)	Ph	H	90	75—76 (76)	A	9·39	
(2)	4-FC_6H_4	H	73	112—113 (110)	A	9·34	
(3)	4-ClC_6H_4	H	95	131—132 (130)	B	9·39	
(4)	4-BrC_6H_4	H	80	137—139 (143)	C	9·40	
(5)	4-MeC_6H_4	H	81	88—89 (78)	A	9·33	2·41 (Me)
(6)	4-MeO·C_6H_4	H	74	109 (101)	C	9·25	3·87 (OMe)
(7)	4-HO·C_6H_4	H	57[e]	143—144	C	9·24	
(8)	4-AcO·C_6H_4	H	83	114—115	A	9·37	2·32 (Ac)
(9)	4-O_2N·C_6H_4	H	83	183—184 (189)	B	9·62	
(10)	4-AcNH·C_6H_4	H	88	163	D	9·33	2·21 (Ac)
(11)	4-PhC_6H_4	H	62	164—165	A	9·42	
(12)	4-F_3C·C_6H_4	H	56	95—97	A	9·52	
(13)	3-HO·C_6H_4	H	71[e]	143—145	C	9·38	
(14)	3-AcO·C_6H_4	H	74	77—78	C	9·40	2·34 (Ac)
(15)	3-O_2N·C_6H_4	H	82	135—136	B	9·61	
(16)	3-AcNH·C_6H_4	H	73	153—154	E	9·41	2·22 (Ac)
(17)	2-FC_6H_4	H	66	50	A	9·67	
(18)	2-O_2N·C_6H_4	H	64	98—99	E	9·35	
(19)	Ph	Cl	26	123—124	C		
(20)	Ph	Me	62	84—85 (81)	E	2·75 (Me)	
(21)	Ph	Ph	82	90—91 (125)	F	7·36 (Ph)	
(22)	4-MeO·C_6H_4	Ph	70	105—106	F	7·36 (Ph)	3·82 (OMe)
(23)	2-Naphthyl	H	87	115—116	C	9·50	
(24)	2-Thienyl	H	50	53—54	C	9·23	
(25)	4-Pyridyl	H	19	150	C	9·68	
(26)	3-Pyridyl	H	42	95	C	9·55	
(27)	2-Pyridyl	H	37	190—192	G	10·09	

[a] Values in parentheses from ref. 1*b*. [b] Solvents: A, cyclohexane, B, $CHCl_3$, C, H_2O–EtOH, D, BuOH, E, EtOH, F, MeOH, G, $CHCl_3$–cyclohexane. [c] H unless stated otherwise. [d] Substituent on aryl group. [e] Obtained directly (see Experimental section).

[2/1979 *Received*, 21*st August*, 1972]