Studies on Heterocyclic Primary Amines, Part II Synthesis of 5-Aryl-2-(diarylphosphoramido) and (p-tolyl Sulfanilamido)-1,3,4-Oxadiazoles

M. EL-DEEK, E.EL-SAWI* AND K. EL-BADRY

Departments of Chemistry, Faculty of Science and University College for Women, Ain-Shams University Cairo, Egypt.

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Summary: 2-Amino-5-Aryl-1,5,3,4-Oxadiazoles have been condensed with diphenylphosporyl chloride and p-toluenesulfonyl chloride to give the corresponding phosphoramido and sulfanilamido derivatives. The di-p-nitrophosphoramido derivatives were prepared from phosphoramidic dichlorides and sodium p-nitrophenate. The structures have been confirmed by correct analytical data and IR spectral studies.

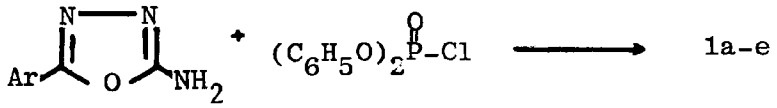
While benzoylation and sulfonation are usually used as a means of characterising and identifing compounds having hydroxy, primary and secondary amino groups, relatively little attention has been directed to organo-phosphorus derivatives for identification of such compounds. This may be due to the poor yields and side reactions encountered when phosphorylation carried out under Schotten-Baumann conditions [1].

In continuation of our previous work on heterocyclic systems bearing phosphorus substituents [2]. We have now synthesized oxadiazole derivatives having a phosphoramido 1,2 and sulfamido 3 moieties attached at position-2.

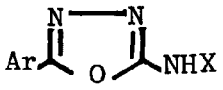
The aim of such investigation was ascertain the possibility of using phosphoryl derivatives in identifying the amino-oxadiazoles 4 a-e and to determine how the sulfonamido and the phosphoramido moieties could affect the biological activity of the oxadiazoles [3-10].

5-Aryl-2-(diphenylphosphoramido)-1,3,4-oxadiazoles 1 a-e were synthesized by refluxing in dry toluene the aminooxadiazoles 4 a-e and diphenylphosphoryl chloride in the presence of tertiary base:

The synthesis of 5-Aryl-2-(di-p-nitrophenylphosphos-phoramido)-1,3,4-oxadiazoles 2 a-e has been best achieved by treating N-(5-aryl-1,3,4-oxadiazol-2-yl) phosphoramidic dichlorides 5 a-e with sodium p-nitrophenate in benzene. The dichlorides 5 a-e were obtained by refluxing aminooxadiazoles 4 a-e with phosphoryl chloride [2].



4a-e



1 : X=$(C_6H_5O)_2P(O)$

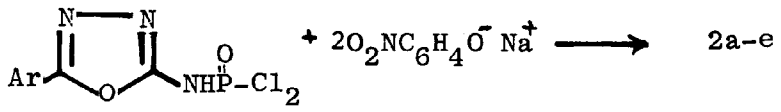
2 : X=$(p\text{-}O_2NC_6H_4O)_2P(O)$

3 : X=$(p\text{-}H_3CC_6H_4)SO_2$

4 : X=H

	Ar
a-	C_6H_5
b-	$m\text{-}ClC_6H_4$
c-	$(p\text{-}ClC_6H_4$
d-	$(p\text{-}CH_3C_6H_4$
e-	$(p\text{-}CH_3OC_6H_4$

*To whom all correspondence should be addressed. Present address: Department of Chemistry College of Science University of Riyadh P.O. Box No: 2455 Riyadh-Saudi Arabia.



5a-e

The condensation of the aminooxadiazoles 4 a-e with p-toluenesulfonyl chloride in the presence of dry pyridine afforded the sulfonamides 3 a-e.

Correct analytical values are in support for the structure assigned for the products 1-3 a-e. Besides, the infrared spectra of all the phosphoramido derviatives 1-2 a-e displayed a strong band around 1250 cm^{-1} due to the P=O stretching vibration IIa in addition to a broad band at 3300 cm^{-1} due to the NH strectching vibration. The strong bands in the region 950 cm^{-1} are due to the P-O-Ar absorption IIb. The sulfanilamido derivatives showed the asymmetric and symmetric stretching modes of vibration of S=O in the range 1380 and 1165 cm^{-1} [12]. The oxadiazole nucleus had characteristic absorption at around 1550 cm^{-1}

All the compounds are new crystalline compounds. A comparison of their melting points reveals that the phosphoramides 1 a-e have the lower melting points than the corresponding sulfonamides. The ease by which phosphoramides 1,2 a-e were obtained may be used for the identification of aminooxadiazoles 4 a-e.

All the compounds were screened in vitro againest Mycobacterium tuberculosis at adose level of M.I.C. 80> g/ml and found to be inactive.

Experimental

Melting points are uncorrected. Infrared spectra were recorded on a Beckman IR-5A unit as KBr pellets. The aminooxadiazoles 4 a-e were obtained by oxidative cyclization of aldehyde semicarbazones [13]. Diphenylphosphoryl chloride was prepared according to the method of Hoeflake [14].

5-Aryl-2-(diphenylphosphoramido)-1,3,4-oxadiazoles 1 a-e

A mixture of diphenylphosphoryl chloride (10 mmol) and aminooxadiazoles 4 a-e (10 mmol) was refluxed in dry toluene (25 ml) in the presence of triethylamine (10 mmol). Refluxing was continued for 8 hr. The reaction mixture was cooled to room temperature, then triethylamine hydrochloride was filtered off. The solvent was removed under vacuum and the solid that left was washed with water and crystallised from ethanol. Yield 60%. Table I represents the physical and analytical data.

5-Aryl-2-(di-p-nitrophenylphosphoramido)-1,3,4-oxadiazoles 2 a-e

To a suspension of freshly prepared phosphoramidic dichlorides (10 mmol) in benzene (25 ml), sodium p-nitrophenate was added. The reaction mixture was refluxed for 6 hr. After cooling to room temperature, the solid product was filtered, dried, and washed with water to remove sodium chloride. It was then crystallised from ethanol. Yield 65%. Table II represents the physical data and elemental analysis.

5-Aryl-2-(p-tolylsulfanilamido)-1,3,4-oxadiazoles 3 a-e

A mixture of aminooxadiazoles 4 a-e (10 mmol), p-toluenesulfonyl chloride, (10 mmol) and dry pyridine (20 ml) was heated on water bath for one hour and kept at room temperature for 12 hr. The reaction mixture was poured on to ice containing a little conc sulfuric acid. The crude product obtained was washed with dilute sodium bicarbonate solution and finally with distilled water. It was crystallised from aqueous ethanol. Table III represents the physical and analytical data of 3 a-e.

Acknowledgement

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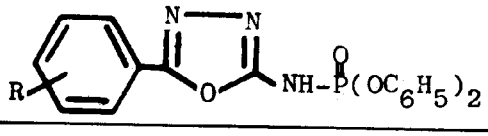
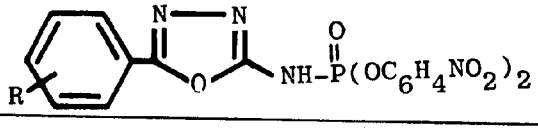
Table 1. 5-Aryl-2-(diphenylphosphoramido)-1,3,4-oxadiazoles 1 a-e.



Compd.	R	M.P. °C	Molecular Formula	Microanalyses Calcd/Found %C	%H	%N
1a	H	161-162	$C_{20}H_{16}N_3O_4P$	61.07	4.07	10.69
				60.83	3.98	10.54
1b	m-Cl	177-178	$C_{20}H_{15}ClN_3O_4P$	56.14	3.50	9.82
				56.03	3.42	9.64
1c	p-Cl	190-192	$C_{20}H_{15}ClN_3O_4P$	56.14	3.50	9.82
				56.49	3.47	10.09
1d	P-CH_3	178-180	$C_{21}H_{18}N_3O_4P$	61.91	4.42	10.31
				61.91	4.23	10.52
1e	p-CH_3O	165-167	$C_{21}H_{18}N_3O_5P$	59.57	4.25	9.92
				59.43	4.26	9.75

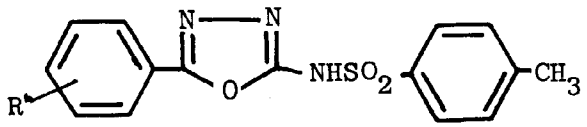
Table 2. 5-Aryl-2-(di-p-nitrophenylphosphoramido)-1,3,4-oxadiazoles 2 a-e.



Compd.	R	M.P. °C	Molecular Formula	Microanalysis Calcd/Found %N	%P
2a	H	223-224	$C_{20}H_{14}N_5O_8P$	14.49	6.42
				14.35	6.50
2b	m-Cl	200-201	$C_{20}H_{13}ClN_5O_8P$	13.53	5.99
				13.75	5.84
2c	p-Cl	214-215	$C_{20}H_{13}ClN_5O_8P$	13.53	5.99
				13.88	6.24
2d[§]	p-CH_3	222-224	$C_{21}H_{16}N_5O_8P$	14.08	6.23
				13.87	6.43
2e	p-CH_3O	209-210	$C_{21}H_{16}N_5O_9P$	13.64	6.04
				13.67	6.29

[§]The composition and purity of compound 2d was also checked by analysis for C & H. Compound 2d requires: C, 50.70; H: 3.21
C, 50.76; H: 3.36

Table 3. 5-Aryl-2-(p-tolylsulfanilamido)-1,3,4-oxadiazoles 3 a-e.



Compd.	R	M.p. °C	Molecular Formula	Microanalyses Calcd/Found %C	%H	%N	%S
3a	H	231-233	$C_{15}H_{13}N_3O_3S$	57.14	4.12	12.22	10.02
				56.91	4.35	13.16	9.98
3b	m-Cl	226-227	$C_{15}H_{12}ClN_3O_3S$	51.50	3.43	12.01	9.15
				51.53	3.39	12.24	9.32
3c	p-Cl	252-254	$C_{15}H_{12}ClN_3O_3S$	51.50	3.43	12.01	9.15
				51.32	3.35	12.15	9.19
3d	p-CH_3	230-231	$C_{16}H_{15}N_3O_3S$	58.35	4.55	12.76	9.72
				58.42	4.54	12.61	9.95
3e	p-CH_3O	234-236	$C_{16}H_{15}N_3O_4S$	55.65	4.34	12.17	9.27
				55.48	4.28	12.09	9.41

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