BRIEF COMMUNICATIONS

ONE-STAGE CONVERSION OF AROMATIC CARBOXYLIC ACIDS INTO 2,5-DIARYL-1,3,4-OXADIAZOLES

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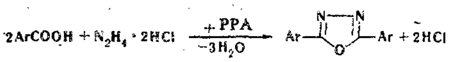
A method has been developed for the one-stage conversion of aromatic carboxylic acids into symmetrical 2,5-diaryl-1,3,4-oxadiazoles by heating them with hydrazine hydrochloride in polyphosphoric acid.

The starting materials for the preparation of 2,5-diaryl-1,3,4-oxadiazoles I are carboxylic acids and hydrazine, which are converted via a number of intermediate stages into N,N'-diaroylhydrazines, the cyclodehydration of which, usually under the action of phosphorus oxychloride, leads to the oxadiazoles.

We have found that it is possible to effect the direct conversion of carboxylic acids into I, with the omission of all the intermediate stages, by making use of the mild but powerful dehydrating action of polyphosphoric acid (PPA) by heating the carboxylic acid and hydrazine hydrochloride in PPA



The oxadiazoles are obtained in fairly pure form and frequently in very high yields, considerably exceeding the over-all yields by the classical method. It has been found possible to obtain in one stage even aminophenyloxadiazoles, which cannot be obtained at all as such by the multistage method and have previously been synthesized only by the transformation of substituents already present in the oxadiazole [1]. It is also possible to obtain hydroxyphenyloxadiazoles, but their synthesis is complicated by the phosphorylation of the phenolic hydroxyls.

The method described here is similar to that given in a British patent [2] which described the production of I from carboxylic acids and previously-prepared hydrazine salts of meta-, pyro-, or polyphosphoric acid. This method involves two stages and starts from the less accessible hydrazine base.

The products that we have obtained are given in the table.

2,5-Diaryl-1,3,4-oxadiazoles

Compound	Reaction conditions		Mp, °C (solvent)	Empirical formula	Found, %			Calculated, %			Yield, %
	Temperature, °C	Time, hr			C	H	N	C	H	N	
2,5-Diphenyl-1,3,4-oxadiazole	130	1,5	137—138* (aqueous ethanol)	$C_{14}H_{10}N_2O$	—	—	—	—	—	—	92
2,5-Di(o-chlorophenyl)-1,3,4-oxadiazole	150—155	1	94—94.5 (aqueous acetone)	$C_{14}H_8N_2Cl_2O$	57.92 57.71	2,63 2,93	—	57.76	2.77	—	96
2,5-Di(o-aminophenyl)-1,3,4-oxadiazole	145	1	201—203 (ethanol)	$C_{14}H_{12}N_4O$	66.64 66.56	4,81 4,92	—	66.65	4.79	—	38.5
2,5-Di(m-methoxyphenyl)-1,3,4-oxadiazole	140—145	1	98—99 (aqueous ethanol)	$C_{16}H_{14}N_2O_3$	68.15 68.39	5.02 5.27	—	68.08	5.00	—	47
2,5-Di(m-nitrophenyl)-1,3,4-oxadiazole	150—155	1	222—223 (aqueous dioxane)	$C_{14}H_8N_4O_5$	53.71 53.83	2.67 2.68	—	53.85	2.58	—	96
2,5-Di(p-chlorophenyl)-1,3,4-oxadiazole	160—170	2	241—242 (dioxane)	$C_{14}H_8N_2Cl_2O$	57.46 57.40	2.75 2.74	9.25 9.26	57.76	2.77	9.62	98
2,5-Di(p-aminophenyl)-1,3,4-oxadiazole	160—170	2	249—250 (ethyl acetate)	$C_{14}H_8N_2Br_2O$	44.13 44.14	2.29 2.11	6.99 7.29	44.25	2.12	7.37	90
2,5-Di(p-bromophenyl)-1,3,4-oxadiazole	140—150	1	251—253 (ethanol)	$C_{14}H_{12}N_4O$	67.18 66.92	5.15 5.27	21.11 21.36	66.65	4.79	22.21	77.5
2,5-Di(p-nitrophenyl)-1,3,4-oxadiazole	160—170	2	314.5—316.5 (dioxane)	$C_{14}H_8N_4O_5$	—	—	17.49 17.57	—	—	17.95	92

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*Identified by a mixed melting point

EXPERIMENTAL

A well stirred and ground mixture of 0.2 mole of carboxylic acid and 0.1 mole of hydrazine hydrochloride was mixed with 8 to 10 times its weight of PPA. The resulting mixture was heated in an open flask with periodic stirring under the conditions given in the table. Then it was poured into a large volume of water and the product that separated out was filtered off, dried, and recrystallized from a suitable solvent. Diaminophenyl-1, 3, 4-oxadiazole was isolated from the aqueous acidic solution by making it alkaline.

REFERENCES

1. A. P. Grekov, O. P. Shvaika, and L. M. Egynova, ZhOKh, **29**, 2027, 1959.

2. Brit. Pat. 896219, 1962; C. A. **58**, 12574, 1963.

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REACTION OF SULFOLENES WITH BENZOYL PEROXIDE AND IODINE

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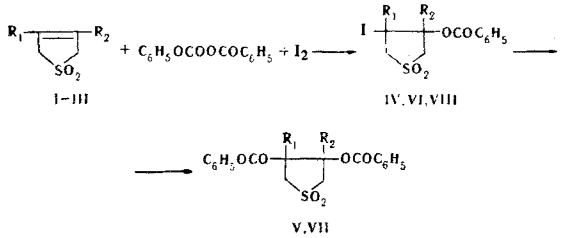
The reaction of 3-sulfolene with benzoyl peroxide and iodine has given 3-benzoyloxy-4-iodosulfolane and 3, 4-dibenzoyloxysulfolane. In the case of 3-methyl-3-sulfolene and 3, 4-dimethyl-3-sulfolene, the corresponding benzoylated iodohydrins have been isolated.

It has been reported previously [1] that 3-sulfolene I reacts with silver benzoate and iodine in a molar ratio of 1:2:1 with the formation of 3, 4-dibenzoyloxysulfolane and a small amount of 3-benzoyloxy-4-iodosulfolane, which can be regarded as the product of the reaction of I with the benzoyl hypoiodite formed by the reaction of silver benzoate with iodine [2]. According to Hammond and Soffer [3], the formation of benzoyl hypoiodite is also assumed in the thermal decomposition of benzoyl peroxide in carbon tetrachloride in the presence of iodine. Consequently, it appeared of interest to study the possibility of the benzoyloxylation of sulfolenes with benzoyl peroxide in the presence of iodine in accordance with the following scheme



I, IV, V $R_1=R_2=H$; II, VI, VII $R_1=H$, $R_2=CH_3$; III, VIII $R_1=R_2=CH_3$

The experiments were carried out in boiling carbon tetrachloride at a molar ratio of sulfolene to peroxide to iodine of 1:1.25:1. It was found that under these conditions the sulfolenes undergo practically no iodination. Decarboxylation of the benzoyl peroxide, accompanied by the formation of iodobenzene and phenyl benzoate takes place to a very small extent (3–5%), as can be judged from the amount of CO_2 formed and from the results of thin-layer chromatography. In the case of **I**, 35% of 3-benzoyloxy-4-iodosulfolane (**IV**) and 22% of 3, 4-dibenzoyloxysulfolane (**V**) were obtained. Since **I** does not react with benzoyl peroxide in the absence of iodine, the formation of **V** must be the result of a secondary reaction of the replacement of the iodine in **IV** by a benzoyloxy radical, the rate of which in this case is somewhat lower than in experiments with silver benzoate and iodine, this apparently being connected with the formation in the latter case of insoluble AgI.

Under similar conditions, 3-methyl-3-sulfolene (**II**) formed 3-benzoyloxy-4-iodo-3-methylsulfolane (**VI**) with a yield of 53%. It was impossible to isolate 3, 4-dibenzoyloxy-3-methylsulfolane (**VII**) although, from the results of thin-layer chromatography, a small amount of it was present in the reaction products. Since the conversion of **II** into **VI** was approximately equal to the total conversion of **I** into **IV** and **V**, it may be considered that a methyl group on the double bond has no appreciable influence on the addition of benzoyl hypoiodite but hinders the formation of **VII**.

In the case of 3, 4-dimethyl-3-sulfolene (**III**), 3-benzoyloxy-4-iodo-3, 4-dimethylsulfolane (**VIII**) was obtained in low yield (11%), which is apparently due to the steric blocking of the double bond by the two methyl groups in a similar manner to the way in which they influence hydrogenation or halogenation reactions [4].

Thus, under certain conditions the sulfolenes can react with benzoyl peroxide and iodine to form benzoylated sulfolane iodohydrins and benzoylated glycols, but the ratio of these two products is determined to a considerable extent by the presence of substituents on the double bond.