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Influence of Solvent from Which Crystals of 2-Amino-5-Aryl-1,3,4-Oxadiazoles Grow on Acetylation Reaction in Solid State

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The phenomenon of reaction anisotropy, i.e. forming of different products on different crystals' facets, is characteristic for 2-amino-5-aryl-1,3,4-oxadiazoles solid-state acetylation. In this case, the ratio of products in reaction yield depends on the form of substrate crystal, hence, on the solvent from which the crystal was grown. This hypothesis was confirmed by acetylation of different substituted 2-amino-5-aryl-1,3,4-oxadiazole crystals obtained from dimethylformamide, butyl alcohol and chloroform.

Keywords: Reaction anisotropy, solid-state acetylation, 2-aminooxadiazoles

1. INTRODUCTION

As the previous paper shows[1], 2-amino-5-aryl-1,3,4-oxadiazoles (1) are the compounds with two nucelophilic reaction centres: nitrogen atom of amino-group and heterocyclic nitrogen atom N3. Solid-state acetylation of 2-amino-5-(4-fluorophenil)-1,3,4-oxadiazole by acetyl bromide vapours results in four products and, moreover, different reaction centres react on different crystal facets: on facets (110) and $(\bar{1}10)$ only amino-derivatives are formed, while on (001) facets – only imino-derivatives.[1] This phenomenon is caused by difference in accessibility to acetylation agent of reaction centres on different crystal facets – acetyl bromide vapours. Unfortunately, we did not succeed in obtaining single crystals of 2-amino-5-aryl-1,3,4-oxadiazoles, large enough to identify solid-state acetylation products on direct facet, except 2-amino-5-(4-fluorophenil)-1,3,4-oxadiazole (1b). However, if this type of reaction anisotropy is inherent in various 2-amino-5-aryl-1,3,4-oxadiazoles crystals, changing the area ratio of crystal facets should lead to regular changes in the reaction products relative yield.

In order to obtain crystals with a different ratio of facets areas we use different solvents: dimethylformamide, butyl alcohol, chloroform. The molecules of the solvent from which the crystals were grown are known to form hydrogen bonds with molecules

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of crystal grown. This phenomenon prevents the forming of hydrogen bonds between the molecules of the crystallising compound. As the molecules in crystal have different orientations to various facets, the possibility of specific solvation on different facets varies greatly. Therefore, inhibition of crystal growth on the most solvated facets takes place. The area of this facet extends because crystal growth goes on in other facets.[2] As it was shown in the paper,[2] crystals of acetamide which have been grown from non-polar solvent, are very long needle shaped crystals. On the other hand, when the polar solvent used was taken, the crystals obtained were short and thick: the acetone-type solvent formed hydrogen bonds with NH-groups, while the methyl alcohol-type solvent formed hydrogen bonds with carbonyl groups. Both cases led to an inhibition of crystal growth on solvated facets and to a formation of short crystals.

The choice of solvent depends on the fact that the aminogroup forms the hydrogen bonds with dimethilformamide and butyl alcohol. In the first case the aminogroup is proton donor, in the second it is proton aceceptor.[3] As a result, the area of the facets on which the aminogroups are localised has to increase, hence the relative yield of amino-derivatives also increases, especially in comparison with crystals grown from chloroform.

2. EXPERIMENTAL SECTION

2.1 Materials

2-amino-5-aryl-1,3,4-oxadiazoles (1a–d) were obtained from corresponding aldehydic semicarbazone cyclization.[4]
2-acetylamino-5-aryl-1,3,4-oxadiazoles (2a–d) were obtained as it was described in paper.[5]

2.2 Acetylation of 2-amino-5-aryl-1,3,4-oxadiazoles in the Solid State

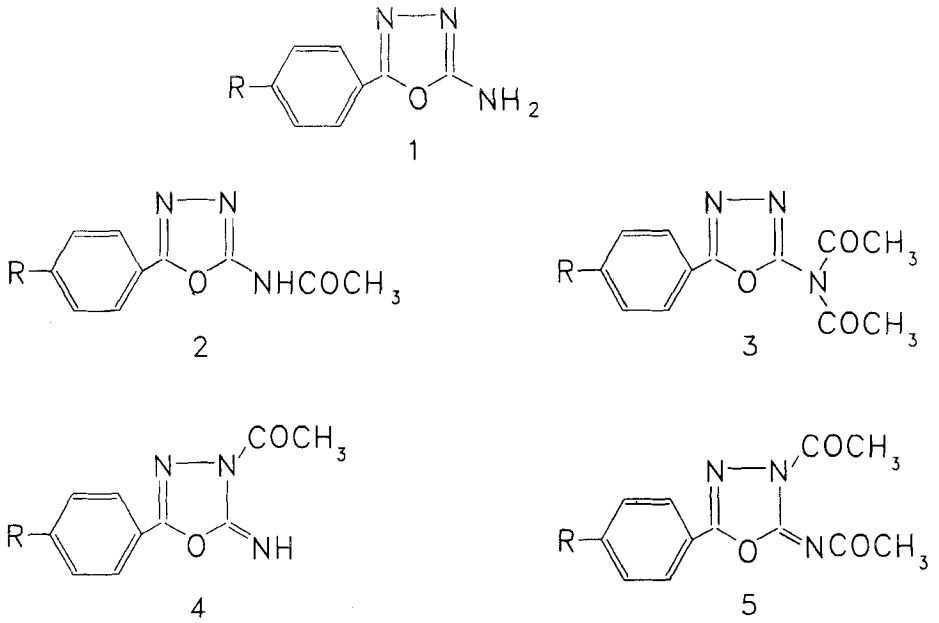
After recrystallising from dimethylformamide, butyl alcohol and chloroform crystals of (1) were exposed under vacuum during 24 h. After that 100 g crystal substrate were put into a reactor and exposed in acetyl bromide vapours at 40°C for two days. After that the acetyl bromide and HBr adsorbed on crystals were removed under vacuum and the crystals were put into gaseous ammonia to prevent reverse reaction.

The initial compound conversion 80–90%. Products were separated by thin-layer chromatography in butyl alcohol–chloroform (1:8) system and were analysed quantitatively using chromatographic thin layer scanner SHIMADZU CS-930 P/N204-03200 by a standard programme. The measurement errors are $\pm$ 10%. Mass-spectra were recorded on a FINNIGAN MAT-90 spectrometer.

3. RESULTS

In the previous paper[1] we have described the chemical structures of 2-amino-5-(4-fluorophenil)-aryl-1,3,4-oxadiazole solid-state acetylation products. Similar evidence can be applied to other oxadiazoles. Taking into account mass-spectra, UV-spectra (Table I) and thin-layer chromatography data (Table II), we conclude that solid-state

acetylation of 2-amino-5-aryl-1,3,4-oxadiazoles leads to the following compounds:



where R = a) H; b) F; c) $N(CH_3)_2$; d) NO_2.

Their relative yields are shown in Table III. During the solid-state acetylation of compound (1) only monoacetyl derivative (2) gives diacetyl derivative (3) and only compound (4) is converted into compound (5).[1] This phenomenon permits us to summarise yields of compounds (2) and (3) and yields of compounds (4) and (5) to calculate the relative of amino- and imino-products, respectively. It is to be noted that the ratio of amono- and imino-products in the yield of the reaction depends on the solvent from which crystals were grown. This ratio decreases from dimethylformamide to chloroform for the different substituted oxadiazole crystals.

4. DISCUSSION

According to Table III, the relative yield of amino-products for all investigated 2-amino-5-aryl-1,3,4-oxadiazoles increases from chloroform grown crystals to dimethylformamide grown crystals. This phenomenon is probably related to the increase of surface area of those facets on which amino-groups are located. Consequently, the same reaction anisotropy takes place for all considered oxadiazoles.

The amino-group nitrogen atoms N2′ is known to be the "hard" centre of ambidental system —N=C—NH_2.[6] Hence, the increase of the negative charge in ambidental

TABLE I

The UV-spectra of 2-amino-5-aryl-1,3,4-oxadiazoles and solid-state acetylation products (λ_{max}, nm)

Compound	1	2	3	4	5
a	290	268	265	230	228
b	288	266	260	230	230
c	230	230	230	235	235
	326	306	315		
d	234	234	234	220	225
	294	306	320	296	296

TABLE II

The R_f^* of 2-amino-5-aryl-1,3,4-oxadiazoles and their acetylation products

Compound	1	2	3	4	5
a	0.17	0.27	0.94	0.53	0.82
b	0.17	0.29	0.90	0.54	0.79
c	0.17	0.30	0.92	0.51	0.80
d	0.27	0.42	0.91	0.51	0.73

* Butyl alcohol–chloroform system (1:8)

system increases the reactivity of the amino-group more than "soft" cyclic nitrogen atom. The data given in Table III corroborate that the increase of the electron-donating nature of the substituent in para-position of the benzene ring raises the amino-group products yield.

The summarising of di- and mono-substituted derivatives allows comparison of the real reactivity of both reaction centres. According to the paper[7] we can use the following equation:

$$\lg\left(\frac{Q_{N2'}}{Q_{N3}}\right) = \lg\left(\frac{Q_{N2'}}{Q_{N3}}\right)_0 + \rho\sigma_N^+ \tag{1}$$

where $Q_{N2'}$ and Q_{N3} are yields of amino- and imino-products correspondingly.

TABLE III

The ratio of amino- and imino-products of acetylation of compounds (Ia–Id) in the reaction yield

Solvent	*a*	*b*	*c*	*d*
Dimethylformamide	5.7	6.1	3.8	9.0
Butyl Alcohol	2.3	3.2	1.6	5.7
Chloroform	1.8	2.2	1.3	4

For solid-state acetylation of crystals grown from different solvents the correlation equations are following.

1) For crystals grown from dimethylformamide:

$$\lg\left(\frac{Q_{N2'}}{Q_{N3}}\right) = 0.73 - 0.15\sigma_N^+, \tag{2}$$

$r = 0.96$; $s = 0.03$; $n = 4$.

2) For crystal grown from butyl alcohol:

$$\lg\left(\frac{Q_{N2'}}{Q_{N3}}\right) = 0.39 - 0.22\sigma_N^+, \tag{3}$$

$r = 0.93$, $s = 0.02$; $n = 4$.

3) For crystals grown from chloroform:

$$\lg\left(\frac{Q_{N2'}}{Q_{N3}}\right) = 0.27 - 0.19\sigma_N^+,$$

$r = 0.98$; $s = 0.02$; $n = 3$.

As has been shown recently, reaction anisotropy in crystals of (1b) is caused by the topochemical nature of solid-state acetylation. Taking into account that data for well

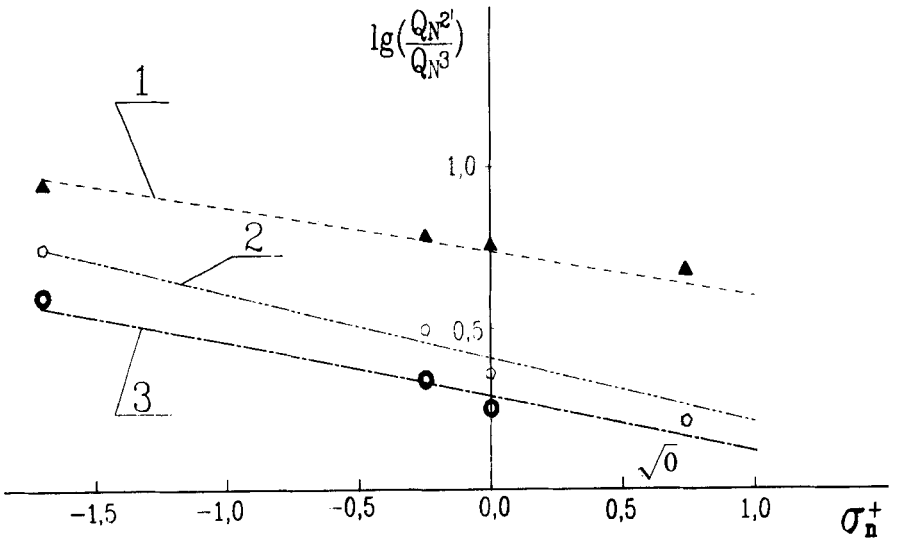


FIGURE 1 Solid-state acetylation of 2-amino-5-aryl-1,3,4-oxadiazole crystals grown from different solvents: 1-dimethylformamide, 2-butyl alcohol, 3-chloroform.

investigated crystals of compound (1b)[1] have correspondence in the equations, one can suppose that reaction anisotropy also takes place for crystals of compounds (1a), (1c), (1d). The fact that the inclination of all lines (Fig. 1) is approximately the same, suggests that all the reacting crystals belong to the same crystal modification. Solvent changing leads to the change of external crystal form, which means that passing from dimethylformamide to teh chloroform the quota of surface of the facets with amino-groups in total crystal surface decreases, and this is true for all compounds discussed. It is worth noting that $\rho < 0$, therefore aminogroup reactivity is accelerated by electrodonating the substitutent more than the reactivity of heterocyclic nitrogen atom.

The correlation equations are approximate and only show the main tendency of solvent and substituent influence on the relative yield of the reaction.

Thus, if the reactive anisotropy takes place in the solid-state reaction, i.e. different crystal products are formed on different crystal facets, the external crystal changing leads to the changing of relative yield of the reaction products.

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