N-Acyl-*a*-aminonitriles in the Pinner Reaction

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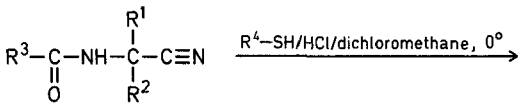
The reaction of thiols with nitriles in the presence of hydrogen chloride, discovered by Pinner[1], gives rise to imidothioesters which are key intermediates in the synthes of dithioesters[2]. However, this method has hitherto only in two cases been successfully applied to the synthesis of N-acyl-α-aminodithioesters[3]; according to our findings, the method cannot be considered a general one for the preparation of the latter class of compounds. Thus, treatment of α-(benzoylamino)-phenylacetonitrile (**1a**, $R^1=R^3=C_6H_5$, $R^2=H$) with hydrogen chloride and an equimolar amount of an alkylmercaptan (ethyl-, pentyl-, benzyl-) led to the formation of the cyclic product **2a** ($R^1=R^3=C_6H_5$, $R^2=H$) in high yield. Compound **2a**

did not undergo thiohydrolysis upon reaction with hydrogen sulfide in pyridine, but was converted into the free 5-amino-2,4-diphenyl-1,3-oxazole (**3a**, $R^1=R^3=C_6H_5$). The assignment of structure **3a** is based on elemental analysis, N.M.R.-, and mass-spectral data. The above described results are in agreement with an earlier report[4]. The same type of reaction was observed by us with compounds **1b–e** (see Table).

On the other hand, N-benzoylaminoacetonitrile (**1f**, $R^1=R^2=H$, $R^3=C_6H_5$) reacted with ethylmercaptan or isopropylmercaptan and hydrogen chloride to give the expected Pinner's products, the imidothioester hydrochlorides **4f** and **4g**, respectively. Compounds **4f** was readily thiohydrolyzed to give the corresponding dithioester (**5f**, **5g**).



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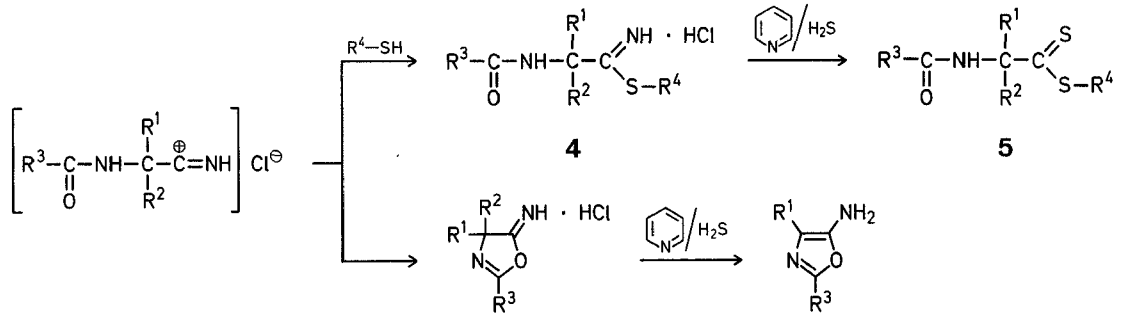

4 **5**

2 **3**

Thus, under the conditions of the Pinner reaction N-acyl-α-aminonitriles react in two different ways: they undergo either intramolecular cyclization or nucleophilic addition of mercaptans, both processes probably involving the same imidoyl chloride as an intermediate. The cyclization reaction appears to be favoured by a polar effect of the group R^3, whereas the addition reaction is apparently sterically hindered by the presence of α-substituents (R^1, R^2). According to our results, the reaction rates are of such a different order that in each case only one product is isolated.

The following procedures are typical.

α-Aminophenylacetonitrile:

A solution of mandelonitrile (100 g, 0.75 mol) in absolute ethanol (1000 ml) is saturated with ammonia and allowed to stand at room temperature for 4 days. The solvent is then removed using a rotatory evaporator. The oily red residue crystallizes on standing; yield: 100 g (100%). Recrystallization of a sample from ether gives the pure product; m.p. 56–57° (Lit. m.p. 55°).

N-Benzoyl-α-aminophenylacetonitrile (1a):

Benzoyl chloride (53 g, 0.38 mol) is added at 0° to a solution of α-aminophenylacetonitrile (50 g, 0.38 mol) and triethylamine (38 g, 0.38 mol) in benzene (250 ml). After 12 hr, the mixture is evaporated to dryness. The residue is washed with water (100 ml) and recrystallized from methanol (250 ml)/carbon tetrachloride (250 ml); yield: 42 g (47%); m.p. 160–160.5°.

5-Amino-2,4-diphenyl-1,3-oxazole (3a):

5-Imino-2,4-diphenyl-4,5-dihydro-1,3-oxazole Hydrochloride (**2a**): A solution of **1a** (1 g, 0.0044 mol) and ethylmercaptan (0.5 ml) in dry dichloromethane (25 ml) is saturated with dry hydrogen chloride for 10 min. The resultant green powder is collected by filtration; yield: 1.10 g (95%); m.p. 130°.

5-Amino-2,4-diphenyl-1,3-oxazole (**3a**): Compound **2a** (1.10 g) is dissolved in dry pyridine and the solution saturated with hydrogen

Table. Products obtained from the Reaction of N-Acyl-α-aminonitriles (**1**) with Mercaptans and Hydrogen Chloride

N-Acyl-α-aminonitrile					Mercaptan	Product of cyclization or addition reaction				Product obtained upon treatment with hydrogen sulfide			
	R^1	R^2	R^3	m.p.	R^4	Reaction conditions	Product	Yield %	m.p.	Reaction conditions	Product	Yield %	m.p.
1a	C_6H_5	H	C_6H_5	160–160.5°	C_2H_5	10 min, 0°	**2a**	95	130° (CH_2Cl_2)	4 hr, 0°	**3a**	42	133–135° (CH_2Cl_2)
1b	C_6H_5	H	CH_3	114–115°	C_2H_5	25 min, 0°	**2b**	95	142–143° (CH_2Cl_2)	4 hr, 0°	**3b**	40	98–99° (CH_2Cl_2)
1c	C_6H_5	H	CF_3	107–109°	C_2H_5	24 days, 25°	**2c**	15	173–175° (CH_2Cl_2)				
1d	C_2H_5	H	C_6H_5	141–142°	C_2H_5	1 hr, 0°	**2d**	60	70° (acetone)		oil, not investigated		
1e	C_2H_5	CH_3	C_6H_5	109–110°	C_2H_5	1 hr, 0°	**2e**	60	145° (acetone)		oil, not investigated		
1f	H	H	C_6H_5	143–144°[1]	C_2H_5	1 hr, 0°	**4f**	85	153° (CH_2Cl_2)	2 hr, 0°	**5f**	40	98–99°[1]
					i-C_3H_7	1 day, 20°	**4g**	60	114–116°				

sulfide during 4 hr at 0°. The solvent is then evaporated in vacuo, the residue washed with water (50 ml), and extracted with dichloromethane. The organic layer is dried ($CaCl_2$) and evaporated to give **3a**; yield: 420 mg (42%); m.p. 133–135°.

$C_{15}H_{12}N_2O$	calc.	C 76.18	H 5.08	N 11.86	O 6.77
(236.3)	found	75.93	5.38	11.76	6.93

Mass spectrum: *m/e* = 236, 206, 180, 105, 77.

N.M.R. (pyridine-d_5): τ = 1.6–1.9 and 2.4–2.8 (m, 1 OH), 2.9–3.5 ppm (m, 2 H).

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