

The Synthesis of 3-Amidino-2-aminopyridine-4-Carboxylates

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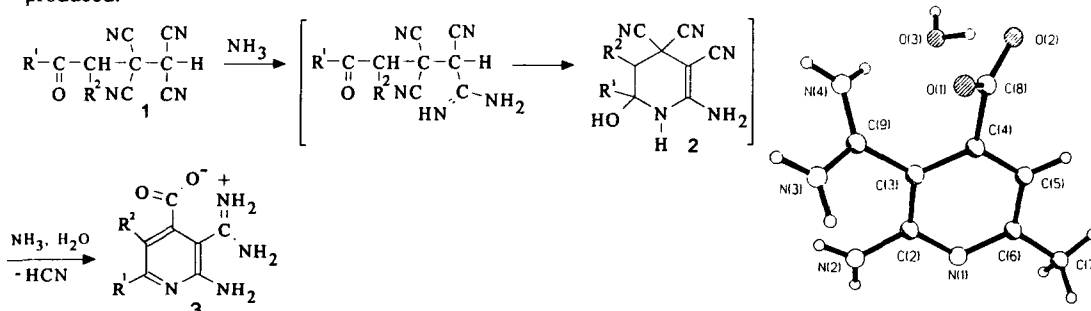
Abstract: A new class of isonicotinic acid derivatives, 3-amidino-2-aminopyridine-4-carboxylates, from aqueous ammonia and $\beta,\beta,\gamma,\gamma$ -tetracyanoalkanes, is reported. © 1997 Published by Elsevier Science Ltd.

The development of new methods of obtaining pyridines with the use of polycyanocarbons is now of great interest¹ and the use of 1,3-dinitriles was known at the beginning of this century.² Coffman's investigation^{3,4} is connected with the development of routes to pyridines. Coffman used more complex polynitriles, 1,1,3,3-tetracyanopropenes and 2-amino-1,3,3-tricyanopropene.

Researchers in our laboratory were the first to use $\beta,\beta,\gamma,\gamma$ -tetracyanoalkanes in the synthesis of pyridines,^{5,7} $\beta,\beta,\gamma,\gamma$ -tetracyanoalkanes being synthesised by interaction of ketones (acetone, methylethylketone) with tetracyanoethylene.⁸

The above-mentioned methods of obtaining pyridines involve transformation of polynitriles under the action of acids.²⁻⁷ All known reactions of this kind involve the interaction of only two nitrile groups. The properties of $\beta,\beta,\gamma,\gamma$ -tetracyanoalkanes with regard to bases are still undiscovered.

We found that when ketones **1** are mixed with aqueous ammonia under mild conditions, pyridine **3** is produced.⁹



1, **3**, R¹=CH₃, R²=H(**a**); R¹=R²=CH₃(**b**); R¹=C₂H₅, R²=H(**c**).

Figure 1. Molecular structure of **3a**.

The structure of compound **3a** was confirmed by X-ray investigation,¹⁰ figure 1.

Initially, addition of ammonia to the γ -CN group and cyclization to oxytetrahydropyridine **2** takes place as in the interaction of ketones **1** with acids.⁵⁻⁷ Then in contrast to the well-known reactions,⁵⁻⁷ an unknown process of formation of COO⁻ and H₂N⁺=C-NH₂ groups from CN groups under the same conditions

takes place. The resulting pyridines **3** containing an amino group and an amidiniocarboxylate fragment form a new type of pyridine undiscovered until now.

Complex transformations which proceed under mild conditions are of great interest. All four nitrile groups take part in the interactions and in a well-known analogous reaction four nitrile groups participate in hydrolysis of tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane-8,8,9,9-tetracarbonitrile.¹¹ The reaction proceeds at high temperature. This process is simpler and could be predicted; the formation of a succinimide ring and two carboxylic groups takes place.

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9. 3-amidino-2-aminopyridine-4-carboxylates **3a-c**. 0.01 Mol of **1a-c** is added to 20ml of 20% aqueous ammonia. The reaction mixture is kept for 48 h at room temperature. The precipitate is filtered and washed with a mixture of 2-propanol and water (1:1). The compound; yield %; m.p. °C; IR (cm⁻¹): **3a**; 75; 298-300; 3530-3500, 1750, 1700, 1620. **3b**; 34; 229-230; 3510-3490, 1750, 1700, 1620. **3c**; 62; 216-218; 3520-3500, 1760, 1700, 1600.
10. Crystal data for **3a**: C₈H₁₀N₄O₂·H₂O, M=212.21, monoclinic, space group P2₁/C at -80°C: a=6.538(3), b=16.996(7), c=8.739(3) Å, β=96.48(3)°, V=965(1) Å³, d_c=1.461 g/cm³, Z=4. 2390 Independent reflections were measured with a Syntex P2₁ automated diffractometer λMoKα, graphite monochromator, θ/2θ-scan, θ_{max}=26°. The factor refinement converged at R=0.038, R_w=0.038 (S=0.55) for 1685 reflections with I>3σ(I). All the calculations were carried out using the SHELXTL PLUS program. Atomic coordinates, bond lengths and bond angles were deposited at the Cambridge Crystallographic Data Centre.
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