



SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NEW (\pm)- α -AMINO NITRILE DERIVATIVES

**N. K. UNDAVIA^{*}, B. S. PATWA^a, H. D. NAVADIYA, A. R. JIVANI
and P. N. DAVE**

Department of Chemistry, Bhavnagar University, BHAVNAGAR – 364002 (Guj.) INDIA

^aDepartment of Industrial Chemistry, Sir P. P. Institute of Science, Bhavnagar University,
BHAVNAGAR – 364002 (Guj.) INDIA

ABSTRACT

The literature survey amply exhibits usefulness of (\pm)- α -amino nitriles with different structural features. To explore new therapeutic agents, We have reported here the preparation and activity of some newly synthesized (\pm)- α -amino nitriles. m-Phenoxy benzaldehyde was converted into hydroxyl-(3-phenoxy-phenyl)-acetonitrile. The elemental analysis supported the constitution of the product. The products were tested for antibacterial, antifungal and insecticidal activity.

Key words : (\pm)- α -Amino nitriles, Antibacterial, Antifungal, Insecticidal.

INTRODUCTION

The wide variety of (\pm)- α -amino nitriles derivatives posses biological activities like antibacterial¹, antifungal² and insecticidal³. Some other workers have also prepared (\pm)- α -amino nitriles and resolved but they have not reported any activity. Undavia et al. ⁴ used acetophenone, KCN and different aryl amines to get (\pm)- α -amino nitriles and resolved them having a p-carboxyl group through brucine salts. Thaker et al. ⁵ prepared and resolved (\pm)- α -amino nitriles from different aldehydes, KCN and glacial acetic acid. They also prepared and resolved N-aryl-D-glucoheptose aminonitriles using glucose as aldehyde component and different amines⁶.

m-Phenoxy-benzaldehyde reacts with potassium cyanide in ethanol to give hydroxyl-(3-phenoxy-phenyl)-acetonitrile (**1**). The compound (**1**) reacts with aromatic amine in alcohol and acid at 15°C for 2 hrs and at room temperature for 24 hrs. to give (3-phenoxy-phenyl)-phenylamino-acetonitrile (**2**). All the compounds synthesized were

^{*} Author for correspondence; E-mail : dr.navadiya@yahoo.com

adequately characterized by their element analysis and spectral data.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. The IR spectra were recorded on Bio-Red FTS-40 spectrophotometer using KBr pellets. The purity of all dyes has been checked by thin-layer chromatography⁶. The absorption spectra of all the compounds were recorded on Beckmann DB-GT Grafting Spectrophotometer.

Hydroxy-(3-phenoxy-phenyl)-acetonitrile⁷ (1)

Potassium cyanide (1.30 g, 0.02 mole) was dissolved in water (4 mL) and cooled below 5°C. To this, freshly distilled m-phenoxy-benzaldehyde (3.96 g, 0.02 mole) in ethanol (25 mL, 95%) was added. The mixture was stirred maintaining temperature below 5°C. To this, glacial acetic acid (1.20 g, 0.02 mole) was added with constant stirring below 5°C to obtain hydroxyl-(3-phenoxy-phenyl)-acetonitrile. The compounds are recrystallised with 95% alcohol. Yield 76%, m. p. 79°C. Anal. Calcd. for C₁₄H₁₂ON : C, 80.00; O, 7.71; N, 06.66. Found C, 80.18; O, 7.70; N, 06.60 %.

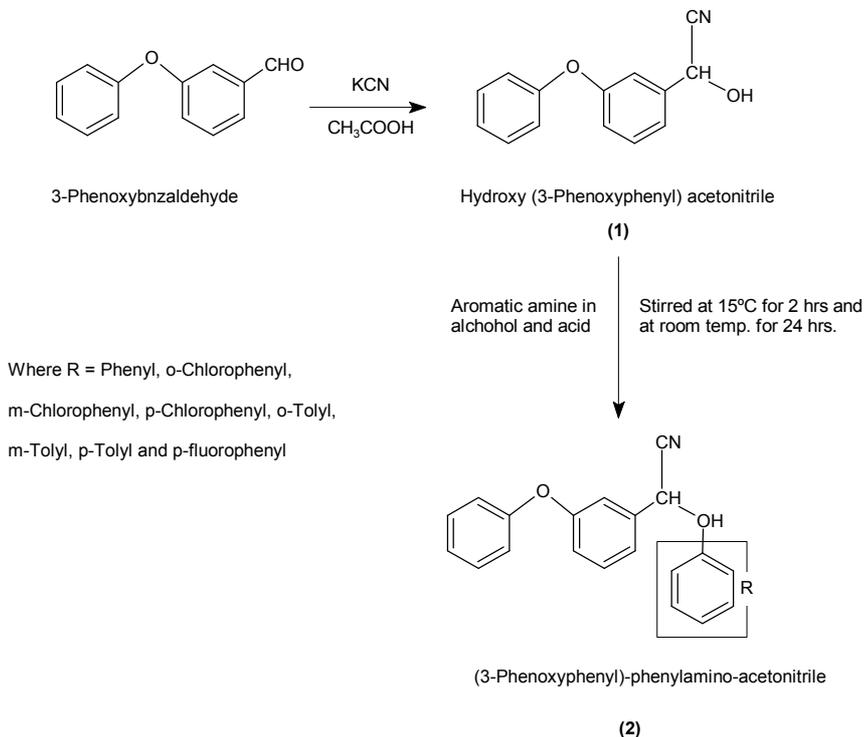
(3-Phenoxy-phenyl)-phenylamino-acetonitrile⁸ (2)

Freshly distilled aniline (0.02 moles 1.86 g) in 10 mL 95% alcohol and 5 mL of acetic acid cooled below 5°C was added with continuous stirring in well ventilated hood to above hydroxyl-(3-phenoxy-phenyl)-acetonitrile. Temperature was maintained at 15°C during addition. The reaction mixture was stirred for further 2 hours and was kept at room temperature (25°C) for 24 hrs to obtain (3-phenoxy-phenyl)-phenylamino-acetonitrile. Long needles were made cyanide and amine free by washing with sufficient diluted hydrochloric acid (0.2 M). The compounds were recrystallised with 95% alcohol. Yield 80%, m. p. 70°C. Anal. Calcd. for C₂₀H₁₆ON₂ : C, 79.98; O, 5.33; N, 09.33. Found C, 79.78; O, 5.56; N, 09.30%. IR : 1669 cm⁻¹ due to -N-H and at 3394 cm⁻¹ due to -N-H 2nd amine. The absorption at 752 and 758 cm⁻¹ is due to mono-substituted and at 822 cm⁻¹ is due to 1, 4-disubstituted benzene ring. The aromatic and aliphatic C-H appeared at 3030 cm⁻¹ and 2920 cm⁻¹, respectively. The absorption at 752 cm⁻¹ is due to one adjacent -C-H aromatic. The absorption at 1655 cm⁻¹ is due to amide carbonyl stretch.

Other compound (3-8) were synthesized similar to (2), respectively. Characterization data are presented in Table 1.

Table 1 : Characterization

Comp.	R	Molecular formula	Yield (%)	M. P. (°C)	Found (%) (Calcd.)		
					C	N	O
1	(a) Phenyl	C ₂₀ H ₁₆ ON ₂	80	70	79.98 (79.78)	09.33 (09.30)	05.33 (05.56)
2	(b) p-Chloro phenyl	C ₂₀ H ₁₅ ON ₂ Cl	78	110	71.75 (71.78)	08.37 (08.32)	04.78 (04.68)
3	(c) m-Chloro phenyl	C ₂₀ H ₁₅ ON ₂ Cl	74	60	71.75 (71.76)	08.37 (08.37)	04.78 (04.69)
4	(d) o-Chloro phenyl	C ₂₀ H ₁₅ ON ₂ Cl	78	70	71.75 (71.71)	08.37 (08.36)	04.78 (04.80)
5	(e) o-Tolyl	C ₂₁ H ₁₈ ON ₂	74	80	80.23 (80.19)	08.91 (08.96)	05.09 (05.10)
6	(f) m-Tolyl	C ₂₁ H ₁₈ ON ₂	78	70	80.23 (80.17)	08.91 (08.86)	05.09 (05.10)
7	(g) p-Tolyl	C ₂₁ H ₁₈ ON ₂	77	100	80.23 (80.20)	08.91 (08.88)	05.09 (05.15)
8	(h) p-Fluorophenyl	C ₂₀ H ₁₅ ON ₂ F	81	80	75.46 (75.24)	08.86 (08.86)	05.03 (05.28)



Scheme

RESULTS AND DISCUSSION

The synthesized (\pm)- α -amino nitriles derivatives were subjected to biological evaluation. The tests were performed to evaluate biological activity against various microorganisms like bacteria, fungus and insects by different methods⁹⁻¹¹.

Table 2 indicates minimum concentration required for inhibiting the growth of *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogenes* and *Pseudomonas aeruginosa*. It can be seen that (\pm)- α -amino nitriles (**1-8**) synthesized using aniline, o/p-chloroaniline, m-tolylamine, p-fluoroaniline, as aromatic amine show good activity against some test species. They required 50 ppm or less concentration for inhibition of bacteria. Compounds synthesized using aniline, m/p-chloroaniline, o/m-tolylamine, 3-chloro-4-fluoro aniline as aromatic amine show moderate activity against some test species. They required 50 to 100 ppm concentration of the compound. While compounds synthesized using o/m/p-chloroaniline, o/m/p-tolylamine, p-fluoroaniline, as aromatic amines show

poor activity or no activity up to 1000 ppm concentration of compound.

Table 2 : Bactericidal evaluation concentration compounds in $\mu\text{g}/\text{mL}$. (Standard drug Gentamycin)

Comp.	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>S. pyogenus</i>
1	100	100	50	50
2	200	500	100	25
3	100	200	200	100
4	200	500	200	50
5	200	200	100	100
6	200	1000	100	50
7	500	500	500	1000
8	200	500	50	12.5
Gentamycin	0.05	1	0.25	0.5

Table 3 indicates minimum concentration required for inhibiting the growth of *Candida albicans*, *Aspergillus niger*, *Aspergillus clavatus*, *Aspergillus flavus*, *Sclerotium sclera*, *Sclerotium rolfsi*, *Collectotrichum logenarium*, *Rhizoctonia solani*, *Fusarium oxysporum*, *Alternaria burnsil* and *Alternaria solani*. It can be seen that (\pm)- α -amino nitriles (**1-8**) synthesized using aniline, o/m/p-chloroaniline, m/p-tolylamine, p-fluoroaniline, as aromatic amines show good activity against some fungi. They required 100 ppm or less concentration for inhibition of fungi. Compounds synthesized using aniline, o/m/p-chloro aniline, o/m-tolylamine, p-fluoro aniline, as aromatic amines show moderate activity against some test species. They required 100 to 500 ppm concentration of the compound. While compounds synthesized using aniline, o/m/p-chloroaniline, o/m/p-tolylamine, p-fluoroaniline, show poor activity or no activity up to 500 to 1000 ppm or more concentration of compound is required.

Table 4 : Insecticidal evaluation concentration compounds in $\mu\text{g/mL}$. (Standard drug Cypermethrine)

Comp.	<i>Heliothus armygera</i>
1	150
2	125
3	100
4	150
5	200
6	150
7	175
8	075
Cypermethrine	025

Table 4 indicates minimum concentration required for inhibiting the growth of *Heliothus armygera*. It can be seen that (\pm)- α -amino nitriles (**1-8**) synthesized using aromatic amines are aniline, o/m/p-chloroaniline, o/m/p-tolylamine and p-fluoroaniline. Compounds with aniline shows poor response on test species; O-Chloroaniline poor response on test species; m-Chloroaniline shows good response on test species; p-Chloroaniline shows moderater response on test species; o-tolylamine shows poor response on test species; m-Tolylamine shows moderate response on test species. p-Tolylamine shows poor response on test species and p-Fluoroaniline shows good response on test species. Compound requiring 100 ppm or less concentration for inhibition of *Heliothus armygera* is said to give good response on test species. Compound requiring 100 ppm to 150 ppm concentration for inhibition of *Heliothus armygera* is said to give moderate response on test species. Compound requiring 150 ppm to 250 ppm or less concentration for inhibition of *Heliothus armygera* is said to give poor response on test species. Compound requiring more than 250 ppm concentration is said to give no response to test species *Heliothus armygera*.

ACKNOWLEDGEMENT

The authors are grateful to Dr. D. R. Korat, Principal, Sir P. P. Institute of Science, Bhavnagar University, Bhavnagar for providing necessary research facilities. Authors are

also thankful to Professor Dr. S. B. Mehta, Head, Dept. of Chemistry, Bhavnagar University, Bhavnagar.

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Accepted : 20.02.2009