ONE POT SYNTHESIS OF α-AMINONITRILE AND α-AMINO ACID FROM SCHIFF BASES

Hashemi, Mohammad M. and Almasi, Behnaz*
Department of Chemistry, Sharif University of Technology, P.O.Box 11365-9516, Tehran, I.R. Iran

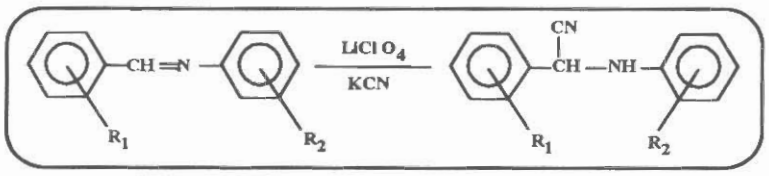
ABSTRACT: *Addition of potassium cyanide to a mixture of Schiff base and lithium perchlorate afforded α-aminonitriles in high yields. Addition of potassium cyanide to a methanolic solution of Schiff base and phosphoric acid afforded α-amino-nitriles. When the reaction mixture was refluxed it gave α-amino acids in high yields.*

KEY WORDS: *α-Aminonitriles, α-Amino acids, Schiff bases.*

Synthesis of unnatural amino acids have been of great interest to organic chemists. The Strecker synthesis is a well-known classical procedure for the preparation of α-aminonitriles by addition of hydrogen cyanide to a Schiff base generated from aldehydes and amines. Hydrolysis of the aminonitriles yields α-amino acids [1-3]. In this method, α-aminonitriles are regarded as the intermediates which should be purified prior to hydrolysis to α-amino acids [4,5].

Lithium perchlorate has been used as a Lewis acid in many reactions [6]. It is reported that Diels-Alder reaction is accelerated in the presence of lithium perchlorate in which lithium functions as the Lewis acid [7]. *Grieco* reported that lithium perchlorate catalyzes Michael reactions including sterically demanding β, β-disubstitued unsaturated carbonyl systems [8].

We now report the synthesis of aromatic α-aminonitriles by addition of potassium cyanide to Schiff bases in presence of lithium perchlorate. Also the synthesis of α-amino acids directly from the Schiff bases is discussed. Aromatic aldehydes and aromatic amines react without complication to form Schiff bases in high yields. A solution of potassium cyanide is added to a mixture of a Schiff base and lithium perchlorate to give α-aminonitriles in high yields. We suggest that lithium functions as a Lewis acid which coordinates with nitrogen atom of the double bond to facilitate the nucleophilic attack by the cyanide ion on the carbon of the double bond of the Schiff base. This is an efficient method for preparation of α-aminonitriles without any concern for the hydrogen cyanide gas. The results are tabulated in Table 1.



* *To whom correspondence should be addressed.*

1021-9986/99/1/33 3/$/2.30

Table 1: Formation of α-aminonitrile from the Schiff bases

Entry	R_1	R_2	α-aminonitrile*		
			mp(°C)	Yield(%)	δ,H benzilic
1	C_6H_5	C_6H_5	83	98	5.4
2	C_6H_5	p-C_6H_4 -OH	122	90	5.2
3	C_6H_5	p-C_6H_4-Cl	81	85	5.4
4	m-$C_6H_4NO_2$	C_6H_5	91	92	5.5
5	C_6H_5	p-C_6H_4O-CH_3	74	90	5.1
6	m-$C_6H_4NO_2$	p-C_6H_4O-CH_3	74	99	5.4

* *I.R C≡N streching appears at around 2238 cm^{-1} in all products*

Synthesis of α-amino acids directly from Schiff bases is also studied. Our method of total synthesis of α-amino acids involves (a) preparation of a Schiff base (b) addition of phosphoric acid and subsequently potassium cyanide solution, and (c) refluxing the reaction mixture to give rise to the corresponding α-amino acids. The results are summarized in Table 2.

EXPERIMENTAL

Preparation of α-aminonitriles: General procedure

The appropriate Schiff base (3 mmol) and lithium perchlorate (3 mmol) were mixed with 20 mL of methanol in a 100 mL round-bottom flask and stirred with a magnetic stirrer. After approximately 5 minutes, potassium cyanide solution (6 mmol in 5 mL water) was added dropwise. Stiring was continued for additional 2 hours and the reaction mixture poured onto crushed ice. The product which was precipitated out was filtered, washed with cold water and crystallized from hot ethanol.

Synthesis of N-4-hydroxy phenyl-2-phenyl glycin: a typical procedure

To a methanolic solution of N-benzilidine-4- hydroxy aniline (3.94 g, 20 mmol in 50 mL), phosphoric acid (5 mL) was added. The reaction mixture was coolded to 0°C and to this potassium cyanide solution (1.095 g, 30 mmol, 10 mL H_2O) was added dropwise with constant stirring during 30 minutes. Phosphoric acid (5 mL) was added and the reaction mixture refluxed for 20 hours. The mixture was cooled to room temperature and extracted with ether (2×25 mL). The excess solvent was removed under reduced pres-

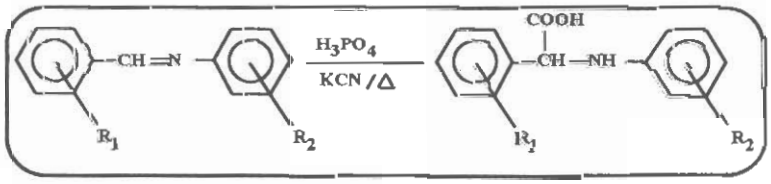


Table 2: Synthesis of α-amino acid from the Schiff bases

Entry	R_1	R_2	mp(°C)	Yield(%)	IR (COO^-NH_2/NH) (cm^{-1})	Mass spec. (m/e)
1	H	p-OH	200	70	1615, 3000-3253	121
2	H	p-Cl	–	60	1661, 2592	139
3	m-NO_2	H	80	60	1615, 3407	105
4	m-NO_2	p-O-CH_3	180	86	1661, 3453	135
5	H	p-O-CH_3	190	86	1623, 2615	135

sure. The residues obtained were crystallized from ethanol-ether (1:3) to give 3.40 g of yellow pale crystalls (70%) mp 200°C.

Received, 15th October 1997; Accepted, 9th November 1998

REFERENCES

[1] Ogata, Y. and Kawasaki A., *J. Chem. Soc.(B),* 325(1971).

[2] Harusawa, S. Hamada Y. and Shiolri T., *Tetrahedron Lett.,* 4663(1979).

[3] Davis, F. A. Reddy, E. R. and Portonovo P. S., *ibid,* 9351(1994).

[4] Patel, M. S. and Worsley, M., *Can. J. Chem.,* **48,** 1881(1970).

[5] Naim S. Khan, N. H. and Siddiqui, A. A., *Indian. J. Chem.,* **19**B, 622(1980).

[6] Grieco, P. A., *Aldrich Chimica Acta,* **24,** 59(1991).

[7] Forman, M. A. and Dailey, W. P., *J. Am. Chem. Soc.,* **113,** 2761(1991).

[8] Grieco, P. A., Cooke, R. J., Henry, K. J. and Vaner Roest, J. M., *Tetrahedron Lett.,* 4665 (1991).