Polyethylene Glycol-mediated Transformation of Aldehydes to Nitriles

Madhavi Latha Duda[1] and Amarnath Velidandi[2*]

***Corresponding author:-**Amarnath Velidandi

[1]Research Scholar, Department of Chemistry, Chaitanya (Deemed to be university),Telangana (State), India.

*[2]Associate Professor, Department of Chemistry, Chaitanya (Deemed to be university), Hanumakonda-506001, Telangana State, India., Email: velidandi@yahoo.co.in.

Abstract

A one-pot procedure is developed for converting aldehydes to nitriles with low cost using aqueous ammonia in Polyethylene Glycol -400 as a reusable solvent. In literature various methods are available for preparing nitriles from aldehydes, many of them were having some limitations. In this method, we observed many advantages than the available methods. In present method achieved excellent yields of nitrile (aromatic/unsaturated) comprising electron-donating (or) electron-withdrawing groups with the simple procedure.

Keywords: aldehyde, transformation, PEG-400, nitrile, triethylamine

DOI Number: 10.14704/nq.2022.20.9.NQ44349 Neuro Quantology 2022; 20(9):3031-3034

The efficient, eco-friendly synthesis of nitriles from aldehydes by ammonium acetate can be performed in presence of iodine and tertiary butyl hydrogen peroxide. Ammonium acetate acts as a nitrogen source, I_2 acts as a catalyst, and tertiary butyl hydrogen peroxide functioned as an oxidant. The effect of substrates on catalytic activity results in aldehydes consisting of electron-withdrawing groups which yield nitriles is faster when compared with electron-donating groups [1]. A method developed to achieve high yields of nitriles using reusable oxidant, rapid route with aldehydes, hexamethyldisilazane (HMDS), and oxo ammonium salt (4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate) which acts as a source of nitrogen. The steps involved in the formation of nitrile, (a) silyl imine formation from HMDS and aldehyde, (b) OXO ammonium salt mediated oxidation of silyl-imine, (c) desilylation [2]. A process for Nitrile synthesis from substituted benzaldehydes using nitroxyl radical catalyzed transition-free aerobic oxidation with a catalytic quantity of 4-AcNHTEMP (4acetamido2,2,6, 6tetramethylpiperidine-N-oxyl), in presence of nitric acid, sodium nitrite, and ammonium acetate [3].

In the presence of Brønsted acid transformation of nitriles takes from aldehydes, (O-acyl oximes) as insitu with O-(4-CF_3-benzoyl)-hydroxylamine (CF_3-BHA) which acts as a source of nitrogen [4].

Transformation of aldehydes into nitriles, a nitrogen source is [(NH_2OSO_3H) hydroxylamine-O-sulfonic acid], the reaction takes place in vinegar with very mild conditions.

In mechanism, the elimination step indicates only nitrile formation but not the intermediate oxime formation [5]. A scheme explores quick reaction times under gentle reaction conditions, a one-pot conversion technique to nitriles from aldehydes with the treatment of $TiCl_4$, and hydroxylamine hydrochloride in pyridine leads to good yields with retention of chirality [6].

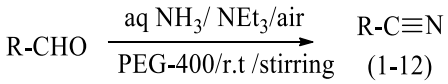
Fast, gentle conversion of aldehyde to nitrile, a broad selection of substituents and tolerable groups for fifty-two derivatives with over 90% yielded by hydroxylamine/sodium carbonate / Difluorosulphonic acid in dimethyl sulphoxide solvent [7].

The transformation with better yields for various substituted Alkyl/aryl aldehydes into corresponding nitriles possible with ammonia - water, ferrous chloride, sodium iodide, and hypo [8]. Selective conversion of nitriles is faster, cheaper, and possible with easily available materials, accessible for distinct groups, like– amide, ester, alcohol, and the pharmaceutically active compounds along with peptides. Mild conditions, redox reaction, acidic, water-oxygen compliant, and easy conversion into other derivatives are advantages with this method [9]. The single step nitriles preparation from

aldehyde using iron penta carbonyle catalysed reaction leads to good yield [10]. Synthesis of Nitrile compounds by using double catalytic system ACT (AcNH-TEMPO) & Rubidium complex, with large range of varieties with more yields can be attained from corresponding aldehydes [11].

A combination of 4-acetamido TEMPO and photo catalysis redox reaction, the oxidation in presence of visible range is possible, Hypo is an effective, low-cost oxidizing agent used as nitrogen producer for the conversion of aldehyde to nitrile with different substrates with more yields [12]. In preparation of nitriles, column purification (or) using costly reagents (or) costly catalysts (or) hectic procedures present in literature, herein we are discussing a simple procedure with good yields.

Scheme:



Plausible mechanism

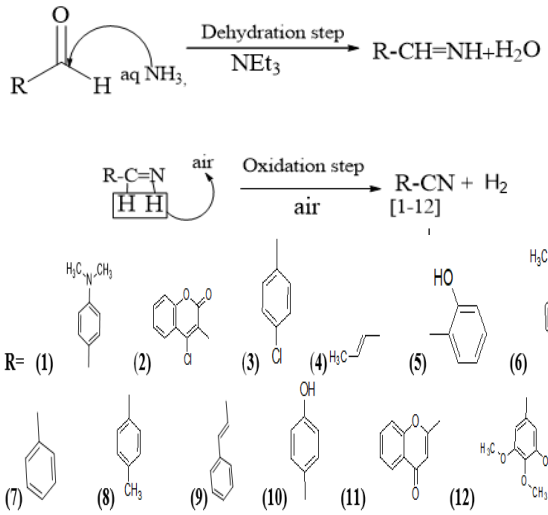


Table: Percentage of yield and reaction time

R-CN	Yield (%)	Reaction time (in minutes)
1	93	120
2	88	105
3	90	110
4	85	130
5	92	140
6	87	110
7	91	135
8	86	145
9	89	155
10	94	135
11	88	120
12	89	150

EXPERIMENTAL SECTION
RESULTS AND DISCUSSIONS:

We purchased all the starting materials from Aldrich Company; checked the reaction development using Thin-layer chromatography by 0.25 mm silica gel plates. In Polyethylene Glycol [PEG-400] medium, aromatic (or) unsaturated aldehyde (1 mmol) and aqueous ammonia (1 mmol), triethyl amine (1 mmol) were taken at room temperature. The resulting suspension stirred in round bottom flask in open air at room temperature, than poured it into crushed ice. (a) Nitrile in solid separated, filtered and dried it (or) (b) Nitrile in liquid form, extracted it in a suitable solvent. It is two step preparations, first step dehydration step, Triethyl amine used as dehydrating agent to remove water molecule to form imine, in second step air acts as oxidising agent to remove hydrogen molecule from imine to get nitrle compound.

Compounds 4, 8, 9, 11, and 12 with allyl, tolyl, cinnamyl, chromonyl, and trimethoxy phenyl groups contained nitriles formed with good yields at more reaction time. Compounds 2 and 6 with coumarinyl, and methoxy phenyl groups contained nitriles formed with good yields at less reaction time. Compounds 1, 3, 5,7and 10 with N,N-dimethyl phenyl , chloro phenyl, 2-hydroxy phenyl, phenyl and 4-hydroxy phenyl groups contained nitriles formed with excellent yields at more reaction time.

All the compounds of this series melting points (or) boiling points are coinciding with existing literature data. The region of nitrile group found in IR (KBr) spectra for all compounds showed nearly 2217 to 2237 cm^{-1}.

Compound 1) 4-(N,N-Di methyl amino) benzonitrile: Solid, m.p 73–75 °C (74–75 °C Balaji etal, *J. Org. Chem* **77** 5364); ^1H NMR

($CDCl_3$) δ 3.0 (2C$\underline{H}_3$, s, 6H), 6.6 (Ar, d, 2H), 7.4 (Ar, d, 2H); M.F: $C_9H_{10}N_2$, (m/z) =146[M^+].

Compound 2) 4-chloro-2-oxo-2H-chromene-3-carbonitrile: (yellow crystal, m.p: 200-201°C (199-200°C, pubchem.ncbi.nlm.nih.gov/compound/4-Chloro-2-oxo-2H-chromene-3-carbonitrile); yield 86%; 'H-NMR ($CDCl_3$): δ 7.4 (Ar, d, 1H), 7.8 (Ar, dd, 1H), 7.9 (Ar, d, 1H), 8.7 (Ar, s, 1H); M.F: $C_{10}H_4ClNO_2$, m/z = 237 [M^++CH_3OH].

Compound 3) 4-Chlorobenzonitrile. White solid; m.p: 94–96 °C (93–94 °C Chaojie etal: *RSC Adv* **7** 1484); ^1H NMR ($CDCl_3$) δ 7.3–7.4 (Ar, m, 2H), 7.5–7.6 (Ar, m, 2H); M.F: C_7H_4ClN, m/z = 137 [M^+].

Compound 4) Crotononitrile: liquid: b.p**:** 120-121 °C(120 °C https://pubchem.ncbi.nlm.nih.gov/compound/2-butenenitrile); ^1H NMR ($CDCl_3$) δ 1.7 (s, 3H), 5.4–6.0 (2H); MF:C_4H_5N, m/z = 67 [M^+].

Compound 5) 2-Hydroxy benzonitrile: m.p: 93-94 °C (92-95 °C Dylan etal *Tetrahedron Letters* **57** 3844); ^1H NMR ($CDCl_3$) δ 6.9 (Ar, d, 1H), δ 7. 0 (Ar, d, 1H), 7.3 (Ar, d, 1H), 7.4 (Ar, d, 1H) δ 8.7 (OH, S, 1H); MF:C_7H_5NO, m/z = 119[M^+].

Compound 6) 4-Methoxybenzonitrile: yellow solid, m.p : 60-62 °C (59-60 °C Sébastien etal *J. Org. Chem.* **77** 9334); ^1H NMR ($CDCl_3$) : δ 3.8 (-O-C$\underline{H}_3$, s, 3H),7.6 (Ar, d, 2H), 6.9 (Ar, d, 2H). MF:C_8H_7NO, m/z = 133 [M^+].

Compound 7) Benzonitrile: m.p: 190-191 °C, colorless liquid, (191°C Sébastien etal *J. Org. Chem.* **77** 9334); ^1H NMR ($CDCl_3$) : δ 7.2 (Ar, m, 1H),7.4-7.3 (Ar, m, 2H), 7.6-7.5 (Ar, d, 2H). MF:C_7H_5N, (m/z): 102(M^+-1).

Compound8)4-Methylbenzonitrile: Colorless oil, b.p:217-218 °C (217 °C https://www.chemsynthesis.com/base/chemical-structure-4122.html); 1H NMR ($CDCl_3$) 2.42 (C$\underline{H}_3$, s, 3H), 7.27 (d, 2H), 7.54 (d, 2H) ; MF:C_8H_7N, m/z =117 [M^+].

Compound 9) Cinnamonitrile: colorless liquid, b.p:262-264 °C (263.8 °C pubchem.ncbi.nlm.nih.gov/compound/Cinnamonitrile#section=Computed-Properties).^1H NMR ($CDCl_3$): δ 5.85 (d, 1H) 7.1 (Ar, m, 1H), 7.2 (Ar, m, 2H), 7.3 (Ar, m, 2H), 7.4(d, 1H). MF:C_9H_7N, (m/z) = 152 [M^++Na].

Compound 10) 4-hydroxybenzonitrile: white solid, MP: 112-113 °C, (111-112 °C, Sébastien; *J. Org. Chem.* **77** 9334). ^1H NMR ($CDCl_3$) : δ 6.9 (Ar, d, 2H), 7.4 (Ar, d, 2H), 9.9 (OH, br s, 1H). MF:C_7H_5NO, (m/z) = 119[M^+].

Compound 11) 4-oxochromene-2-carbonitrile: light yellow solid, M.P: 140-141°C : ^1H NMR ($CDCl_3$) : δ 6.9 (Ar, d, 1H), 7.4 (Ar, m, 1H), 7.5 (Ar, s,1H),7.7 (Ar, m, 1H), 7.9 (Ar, m, 1H). EI-MF:$C_{10}H_5NO_2$, (m/z) = 171[M^+].

Compound12) 3, 4, 5-Trimethoxybenzonitrile: Colorless solid: mp 96–97 °C (95–96 °C Balaji etal, *J. Org. Chem* **77** 5364) ; ^1H NMR ($CDCl_3$) δ 3.8 (s, 6H), 3.9 (s, 3H), 6.8 (s, 2H); MF:$C_{10}H_{11}NO_3$, (m/z) = 216 [M^+ + Na].

CONCLUSIONS

The Nitriles play a crucial role to prepare medicinallyimportantcarboxylicacids/imines/amines. The advantages of the present procedure are 1) ambient reaction temperature 2) high yield production with easily available reagent, and solvent 3) easy isolation of the target product 4) aldehydes with different substitutions can easily convert to nitriles.

ACKNOWLEDGMENTS

The author expresses his sincere gratitude to Prof. P. V.Srilakshmi, National Institute of Technology, Warangal, Prof. B. Prasanna Kumar (late), and Dr. K. Jagadeeshwar for their encouragement and suggestions in the research work.

FUNDING

Author did not receive any funding for this research work.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

REFERENCES

Fang C., Li M., Hu X., Mo W., Hu B., Sun N., Jin L., Shen Z., RSC Adv., 2017, vol. 7, p. 1484–1489. https://doi.org/10.1039/C6RA26435B

Kelly C.B., Lambert K.M., Mercadante M.A., Ovian J.M., Bailey W.F., Leadbeater N.E., Angew. Chem. Int. Ed., 2015, vol. 54, p. 4241–4245. https://doi.org / 10.1002/anie.201412256

Noh J.-H., Kim J., J. Org. Chem., 2015, vol. 22, p. 11624–11628. https://doi.org/10.1021/acs.joc.5b02333

An X.-D., and Yu S., Org. Lett., 2015, vol. 17, p. 5064–5067. https://doi.org/10.1021/acs.orglett.5b02547

Quinn D.J., Haun G.J., Moura-Letts G., Tetrahedron Lett., 2016, vol. 57, p. 3844–3847.http://doi .org/10.1016/j.tetlet.2016.07.047

Leggio A., Belsito E.L., Gallo S., Liguori A., Tetrahedron Lett., 2017, vol. 58, p. 1512–1514. http://dx.doi .org/10.1016/j.tetlet.2017.03.007

Fang W.Y., Qin H.L., J. Org. Chem., 2019, vol. 84, p. 5803–5812. https://doi.org/10.1021/acs.joc.8b03164

Chen H., Sun S., Xi H., Hu K., Zhang N., Qu J., Zhou Y., Tetrahedron Lett., 2019, vol. 60, p. 1434–1436. http://doi10.1016/j.tetlet.2019.04.043

Gurjar J., Bater J., Fokin V.V., Chem. Eur. J., 2019, vol. 25, p. 1906–1909. http://doi10.1002/chem.201805175

Afanasyev O.I., Zarochintsev A., Petrushina T., Cherkasova A., Denisov G., Cherkashchenko I., Chusova O., Jinho O., Man-Seog C., Usanov D.L., Semenov S.E., Chusov D., Eur. J. Org. Chem., 2019, vol. 2019, p. 32–35. http://doi 10.1002/ejoc.201801412

Nandi J., Witko M.L., Leadbeater N.E., Synlett., 2018, vol. 29, p. 2185–2190. http://doi10.1055/s-0037-1610272

Nandi J., Leadbeater N.E., Org. Biomol. Chem., 2019, vol. 17, p. 9182–9186. http://doi10.1039/c9ob01918a