



Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Short Communication

OCAIJ, 6(1), 2010 [83-85]

One-pot conversion of carboxylic acids into nitriles catalyzed by PEG 400 under microwave irradiation

Yu-Qing Cao*, An-Li Qu, Rui-Yan Liu, Chun-Ming Duan
 College of Pharmacy, Hebei University, Baoding-071002, (P.R.CHINA)
 E-mail : pharm_hbu@yahoo.com

Received: 7th January, 2010 ; Accepted: 17th January, 2010

ABSTRACT

Carboxylic acids were converted into nitriles by one-pot reactions with hydroxylamine hydrochloride and zinc catalyzed by PEG400 under microwave irradiation in good-excellent yields.

© 2010 Trade Science Inc. - INDIA

KEYWORDS

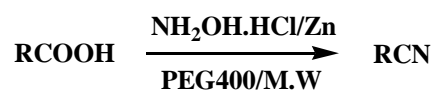
Carboxylic acids;
 Nitriles;
 Hydroxylamine hydrochloride;
 PEG 400;
 Microwave.

INTRODUCTION

Nitrile is a key compound for organic synthesis, and it also serves as an important synthetic intermediate for pharmaceuticals, agricultural chemicals, dyes, and material sciences. A number of methods are known for the conversion of carboxylic acids into nitriles. The primary methods are acid-nitrile exchange reaction^[1]; acid chloride react with sulfonamide^[2]; carboxylic acids treat with urea and sulfamic acid^[3-7], ethyl carbamate and thionyl chloride^[8] or diphosphorus tetraiodide and ammonium carbonate^[9]. However, a number of drawbacks may be encountered in using some of these reagents, such as low yields, harsh reaction conditions, tedious work-up procedures, opaque reaction mechanisms and various limitations. In addition, some of them are corrosive, toxic, expensive or commercially unavailable.

In recent reports, microwave irradiation had been widely applied in organic synthesis^[10-12]. It had been reported that microwave activation for the one-pot synthesis of nitriles from aldehydes^[13-15]. However, only one reaction about conversion of carboxylic acids into

nitriles under the microwave was found by our team, and carboxylic acids is more steady, extensive and inexpensive compared with aldehydes. We now wish to report another new method for the one-pot conversion of carboxylic acids into nitriles catalyzed by PEG 400 with hydroxylamine hydrochloride as amidation reagent and zinc as reductant under microwave irradiation. In this method, the yields are much higher for some products and save much time with comparison to the general methods. The results shown in TABLE 1 and reaction as follow:



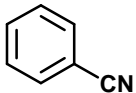
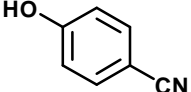
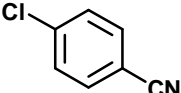
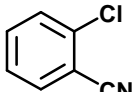
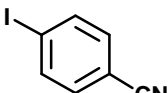
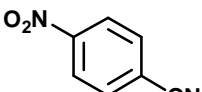
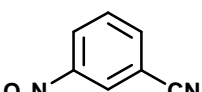
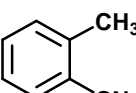
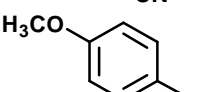
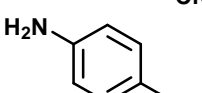
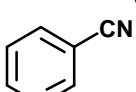
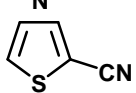
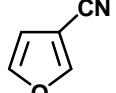
Scheme 1

RESULTS AND DISCUSSION

These reactions are very difficult, even no react if have no catalysts. PEG400 as phase transfer catalyst to this reaction has been studied and the best amount is 5mol%. It was found that lower dosage of PEG 400

Short Communication

TABLE 1 : Conversions of carboxylic acids into nitriles

Entry	Nitriles	Time (min)	Yield (%)	m.p./°C	
				Found	Report ^[3,7,16]
1 ^a		20	91	187-9	188-191
2		17	88	110-112	110-113
3		22	87	92-95	94-96
4		23	88	43-45	43-46
5		21	86	126-128	128-129
6		27	84	146-149	146-149
7		27	85	115-117	115-117
8 ^a		19	91	204-206	205
9		14	93	55-57	57-59
10		25	80	83-85	83-85
11		25	85	50-51	50-52
12 ^a		14	90	190-192	192
13 ^a		16	90	149-151	151

^aBoiling points were determined. Higher power could not catalyze the reaction effectively and higher dosage would undoubtedly lead to more loss of products during the washing procedure.

As shown in TABLE 1, most of aromatic carboxylic acids could be converted to corresponding nitriles in good-excellent yields. The aryl carboxylic acids with

TABLE 2 : Effect of the power to benzoic acid

Entry	Power(W)	Time(min)	Yield(%)
1	119	20	45
2	119	30	57
3	119	40	61
4	231	15	78
5	231	20	93
6	231	25	92
7	385	10	55
8	385	15	63
9	385	20	62

electron-donating groups such as $-\text{CH}_3$ and $-\text{OCH}_3$ were more reactive than those with electron-withdrawing groups such as $-\text{Cl}$, $-\text{I}$, $-\text{NO}_2$ in the aromatic ring, mainly because electron-donating groups increased the electron density of carbonyl and caused the reaction easier. The group of amino as an electron-donating group made 4-aminobenzonitrile (**10**) a lower yield than others, since it is like a nitro under acidic conditions 20 minutes under the power of 231 watt. The causation may be that the higher power input and with the prolongation of time, the temperature is too high to make the reaction effectively carry through, and hydroxylamine hydrochloride would be decomposed in the higher power at the same time; On the other hand, lower power input and shorter reaction time is unable to progress completely. Condition; also because of the reduced solubility and lower reactivity of the zwitterionic amino acid compared with the other substrates. Excellent yields could be obtained in the reactants of heteroaromatic carboxylic acids especially 2-thiophenecarbonitrile (**12**) and 3-furonicarbonitrile (**13**). We propose that the main reason for the high yield may be the more electron their own than benzene ring.

In TABLE 2, the power had an obvious effect to the yields. The most suitable condition was

EXPERIMENTAL

All reactions were performed in a commercial domestic microwave oven (Midea PJ21C-BF). The reaction process was monitored by GF254 thin layer chromatography (TLC) using petroleum ether/ethyl acetate (10:1 v/v) as eluent. Melting points were determined on a microscopy apparatus (SGW X-4) and uncorrected. ¹H-NMR spectra were obtained on a Bruker

Short Communication**ACKNOWLEDGEMENTS**

We thank the Hebei Province Science and Technology Agency (grant No. 4213006) for financial support.

REFERENCES

AVANCE (400MHz) spectrometer using TMS as internal standard and CDCl_3 as solvent. IR spectra were recorded on a Bio-Rad FTS-40 spectrometer (KBr). All the liquid parent materials are fresh distilled. The products were also characterized by comparison of their Melting points and boiling points with the literature values.

General procedure for the preparation of benzonitrile (entry 1, TABLE 1)

A mixture of benzoic acid (2.44g, 20mmol), hydroxylamine hydrochloride (2.09g, 30mmol), zinc dust (1.96g, 30mmol) and PEG400 (5mol%) was irradiated at middle low power (231W) for a period of 20 min. Upon completion, the solids were filtrated and washed with dried dichloromethane ($2 \times 10\text{ml}$). The organic phase was washed with H_2O ($3 \times 10\text{mL}$), dried with magnesium sulfate. After solvent was removed by distillation, the benzonitrile 1.88g (91% yield) was collected at 186-189°C by distillation at atmospheric pressure. $^1\text{H NMR}$ (CDCl_3): δ 7.44 (d, 2H, $2 \times \text{CH}$), 7.51 (d, 2H, $2 \times \text{CH}$), 7.54 (t, 1H, CH); IR (KBr): ν 3067, 2229, 1599, 1490, 1447, 1287, 1223, 1178, 1070, 1026, 927, 760, 688, 548cm^{-1}

CONCLUSION

In summary, a new method for the conversion of carboxylic acids into nitriles catalyzed by PEG 400 under microwave irradiation in satisfactory yields with hydroxylamine hydrochloride as amidation reagent and zinc as reductant is developed. This method is inexpensive, practical and with the less pollution and ease of work-up.

- [1] D.A.Klein; *J.Org.Chem.*, **36**, 3050 (1971).
- [2] A.Hulkenberg, J.J.Troost; *Tetrahedron Lett.*, **23**, 1505 (1982).
- [3] D.H.Liao, Q.M.Xu, Z.H.Xue; *Journal of East China University of Science and Technology*, **23**, 426 (1997).
- [4] B.Yi, Z.P.Tang, Y.B.Lin; *Dyestuff Industry*, **38**, 37 (2001).
- [5] H.Chen, H.B.Li, X.H.Liu; *Journal of Huai Hai Institute of Technology*, **8**, 50 (1999).
- [6] B.Yi, Z.P.Tang, Y.B.Lin; Z.Zeng; *Chemical Research and Application*, **13**, 213 (2001).
- [7] D.H.Liao, B.Wu, *Hua Xue Shi Jie*, **7**, 373 (2000).
- [8] Y.Q.Cao, Z.Zhang, Y.X.Guo; *J.Chem.Technol. Biotechnol.*, **83**, 1441 (2008).
- [9] V.N.Telvekar, R.A.Rane; *Tetrahedron Lett.*, **48**, 6051 (2007).
- [10] Y.W.Sha, T.Han, L.Shen, R.Chen; *Speciality Petrochemicals*, **6**, 21 (2000).
- [11] J.Wang, F.C.Jiang; *Chinese Journal of Organic Chemistry*, **22**, 212 (2002).
- [12] R.Q.Li, H.Yan; *Chinese Journal of Synthetic Chemistry*, **13**, 597 (2005).
- [13] D.S.Bose, A.V.Narsaiah; *Tetrahedron Lett.*, **39**, 6533 (1998).
- [14] J.C.Feng, B.Liu, L.Dai, N.S.Bian; *Synth.Comm.*, **28**, 3765 (1998).
- [15] E.Veverkova, S.Toma; *Synth.Comm.*, **30**, 3109 (2000).
- [16] W.Martha, B.Susan, F.B.Rosemary, S.E.Otterbein; *The Merck Index*, 13th Edition, (2006).