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Exploiting the cyanation ability of O-tosyl hydroxyl amine with variety of aldehydes

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Abstract : The Present article emphasis the prominent and smooth conversions of aldehydes to cyanides by simply heating aldehydes and O-Tosyl hydroxyl amine (NH_2OTs) as a nitrogen donor using toluene as a solvent. The scheme accomplished with excellent yields for a variety of straight chain and aromatic aldehydes, as well as for sterically crowded and conjugated ones with excellent purityand productivity. The reaction conditions worked out well in presence of wide range of functionalities. The advantages of this protocol such as simple and moderate conditions, excellent yields, and good functional group tolerance , may lead to application of this method for the synthesis of nitriles in the synthetic chemistry area.
Keywords : Aldehydes, Cyanation ,O-Tosyl hydroxyl amine, synelimination.

Introduction:

The development of cyanation protocols for the introduction of cyano groups into functionalized aliphatic as well as aromatic compounds is of great concern for organic chemists because nitriles not only present broadly as key molecular scaffold in various natural products[1], biologically active molecules[2-5],industrially significant compounds such as pharmaceuticals[6-7], agrochemicals[8-9], and dyes[10] but also can be transformed into variety of functional groups, such as aldehydes, amines, azoles, amides, and other carboxy functionalities.

Sandmeyer[11-14] and Rosenmund-von Braun[15-17] reactions are the well known traditional methods for the introduction of cyano entity, in which CuCNis used as a cyanating agent in stoichiometric quantities.

Transition metals mediated procedures involving Cu,Niand Pd[18-20]species also serve as attractive unfortunately expensive synthetic routes for the preparation of nitriles, moreover added problem with these is the high affinity of the cyanide ion for the transition metal, which very often results in rapid deterioration of the sensitive and expensive catalyst. Furthermore, most of the cyano sources, specifically KCN, CuCN ,$Zn(CN)_2$, have infamous toxicity, usually involve harsh reaction conditions and exhibit limited functional group tolerance. The dehydration of amides or oximes,[21-26] generally involve complicated operations, heavy metal waste, toxic reagents or harsh reaction conditions .In recent decades, aldehydes have been used as ideal synthetic precursors for nitriles due to their ready availability and ease of use[27-40]

To overcome these shortcomings, we herewith offer a sturdy and competent cyanation protocol using O-Tosyl hydroxyl amine as a source of nitrogen resulting in the activated oxime ester functionality which subsequently undergoes thermally induced syn elimination of PTSA resulting in the formation of nitriles.

Materials and Methods:

Reagents and Chemicals

All other reagents were obtained from commercial sources and used without further purification. All reactions were carried out in oven-dried, glassware. Thin layer chromatography (TLC) was performed on EMD precoated plates and column chromatography was performed on 200-300mesh silica gel.. 1H NMR and 13C NMR spectra were recorded on Varian or Bruker 400 MHz, or 500 MHz spectrometers. Infrared (IR) spectra were recorded on perkinelmers spectrophotometer and are reported as wavenumber (cm–1). Chemical shifts are reported in parts per million (δ) and coupling constants (*J*) are in hertz.Data are reported as follows: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet), coupling constant (J/Hz) .

Optimization conditions:

Typical Procedures for One-Pot Cyanation of Aldehydes: Preparation of benzo nitrile: To aldehyde(1.0mmol) and NH_2OTs (1.2mmol) were mixed in toluene and heated to 80-85^oC for 5-6h and After being heated, the reaction was allowed to cool to room temperature and then diluted by addition of Et_2O (20 mL) and saturated aq$NaHCO_3$ to remove the (PTSA) acid. The layers were separated, and the organic layer was washed successively with saturated aq $NaHCO_3$ and brine (2 × 10 mL). All of the organic layers were combined and then dried (Na_2SO_4). The solvents were removed by rotary evaporation, and the crude residue was purified by column chromatography.

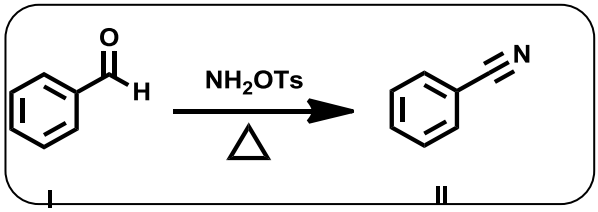
Result and Discussions:

Reaction of O-Tosyl hydroxyl amine with an aldehyde would form an activated oxime ester and which on subsequent heating results in the formation of cyanide looking at this we reasoned that syn/pyrolytic elimination must be the course of this reaction giving the cyanides as the ultimate products .We were pleased to note that electronic parameters didn't affect much during the course of reaction giving good to excellent yields.

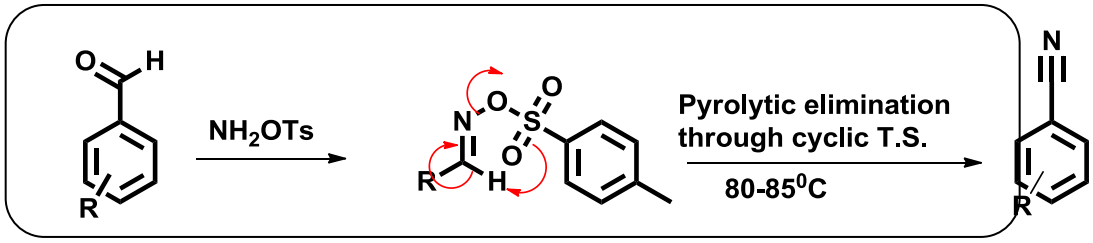
All reactions were monitored by TLC(10% ethyl acetate-Hexane)and there are enough evidence to confirm the structures of the synthesized nitriles. For this purpose, all purified products were characterized by comparison of their melting points ,and FT-IR with those of authentic samples.

In the FT-IR spectrum, a strong sharp absorption band at 2260–2200cm^{-1} was assigned to the CN group of nitriles. The data is reported in**Table1**

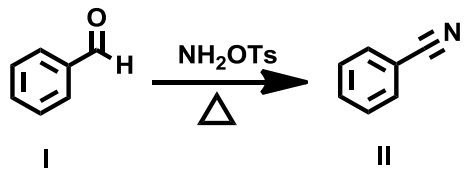
Reaction conditions: Aldehyde (1*mmol*), and NH_2OTs (1.2*mmol*) in toluene were heated at 80-85^0C for 5-6 Hrsas shown in **Scheme 1**. Isolated yields, Reaction crude was purified by standard silica gel chromatography.



Scheme:1Cyanation of aldehydes using O-Tosyl hydroxyl amine

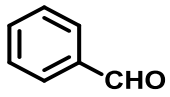
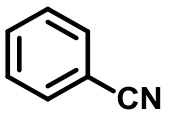
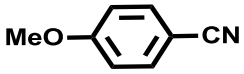
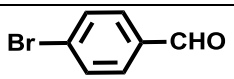
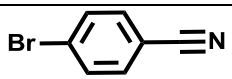
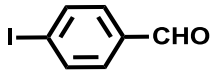
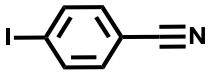
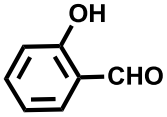
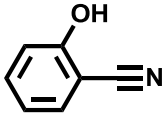
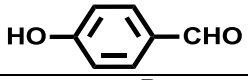
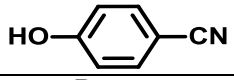
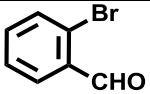
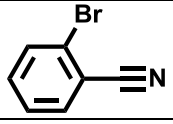
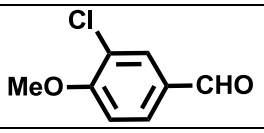
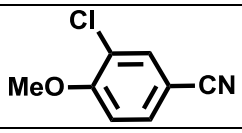
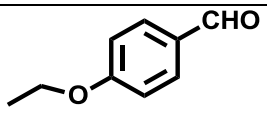
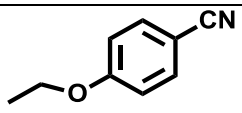
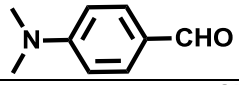
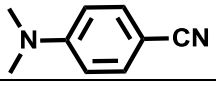
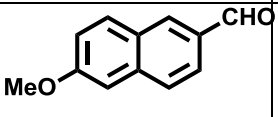
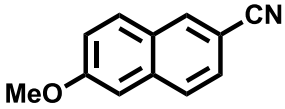
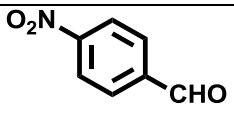
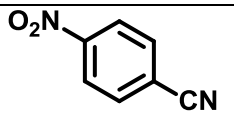
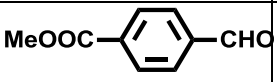
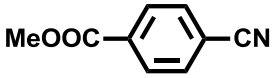
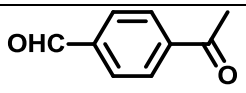
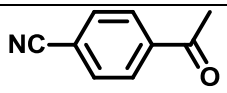


Scheme:1Plausible mechanism for cyanation of aldehydes using O-Tosyl hydroxyl amine
R= (EDG/EWG)



I II

Table-1conversion of aldehyde to nitriles

Entry	stoichiometry		Aldehyde	Final product	MP^{0}C BP	% Yield
	Aldehydes	NH2OTs				
1	1	1.2			188-190	78
2	1	1.2			55-57	85
3	1	1.2			106-108	82
4	1	1.2			125-126	86
5	1	1.2			93-94	80
6	1	1.2			110-112	86
7	1	1.2			54-56	78
8	1	1.2			108-110	75
9	1	1.2			55-57	84
10	1	1.2			70-72	88
11	1	1.2			105-107	80
12	1	1.2			148-150	75
13	1	1.2			65-66	78
14	1	1.2			56-58	82

All the reactions were performed at 80-85^{0}C temperature for 5-6 hrs using aldehyde (1*mmol*)and 1.2 *mmol*of NH_2OTs in toluene.

Analytical data of representative compounds from **Table 1**

Compound 1.Benzonitrile :1H NMR δ 7.66-7.64 (m, 2H), 7.60 (t, J = 7.6 Hz,1H), 7.47 (t, J = 7.6 Hz, 2H). 13C NMR δ 132.77, 132.17, 129.12, 118.85, 112.48.IR (KBr): 2228, 1599, 1491,1446, 1286, 1026, 928, 758, 689, 548 cm-1.

Compound 2.p-methoxybenzonitrile:1H-NMR: δ = 3.84 (s, 3H),6.93 (d, 2H, *J* = 8.9 Hz), 7.57 (d, 2H, *J* = 8.9 Hz); 13C-NMR δ = 55.48, 103.88,114.69, 119.17, 133.91, 162.78. IR (KBr):, 2234, 1765, 1586, 1460, 1406, 1100,950,812, 756 cm-1.

Compound 3.p-Bromobenzonitrile:1H NMR *δ* = 7.60 (d, *J* =8.0 Hz, 2 H), 7.50 (d, *J* = 8.0 Hz, 2 H). 13C NMR *δ* =133.3, 132.6, 127.9, 118.0, 111.2. IR (KBr): 3087, 2923, 2851, 2225, 1711, 1582, 1536, 1475, 822, 540 cm-1.

Compound 4.p-Iodobenzonitrile:1H NMR *δ* = 7.85 (d,*J*= 8.3 Hz, 2 H), 7.37 (d, *J* = 8.3 Hz, 2 H). 13C NMR *δ* = 138.5, 133.1, 118.2, 111.7, 100.3. IR (KBr): 2919, 2850, 2225, 1702, 1542, 1470, 1388, 792, 546 cm-1.

Compound 5.o-Hydroxybenzonitrile:1H NMR *δ* 7.48(m, 2 H), 6.99 (m, 2 H), 6.56 (s, 1 H). 13C NMR *δ* 158.5, 134.8, 132.9,121.0, 116.6, 116.3, 99.4. IR (KBr): 3098, 2923, 2853, 2232, 1768, 1588, 1470, 1402, 952,813, 757 cm-1.

Compound 6.p-hydroxybenzonitrile:1H NMR *δ* 7.55 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 9.0 Hz, 2H), 6.77 (br, 1H).13C NMR δ 160.11, 134.3, 118.8, 116.4, 102.0. ; IR KBr) ν 3124, 2223, 1522, 1335, 1092,752 ,545cm-1.

Compound 12.p-Nitrobenzonitrile :1H NMR :*δ* 8.34 (d, *J* = 8.5 Hz, 2H), 7.87 (d, *J* = 8.5 Hz, 2H).13C NMR :150.0,132.4, 123.8, 118.3, 116.8 (CN).IR (KBr): 3094, 2925, 2840, 2228, 1764, 1580, 1470, 1401, 952,810, 754 cm-1.

Compound 14.p-acetylbenzonitrile:1H NMR δ 8.03 (d, *J* = 8.5 Hz, 2H), δ 7.76 (d, *J* = 8.5 Hz, 2H), δ 2.65 (s, 3H).13C NMR 196.3, 139.7, 132.4, 128.7, 117.8, 115.8, 26.4. IR (KBr):, 2234, 1730, 1588, 1478, 1402, 952,810, 752 cm-1.

Conclusion:

In summary, we have described a sturdy protocol for synthesis of nitriles from commercially available or easily prepared aldehydes using O-tosyl hydroxyl amine as a nitrogen donor by simply heating the reaction mass at moderate temperatures to effect the transformation to the nitriles. Furthermore, the substitution patterns on the aromatic ring do not affect the efficiency of the reaction as well permit for the incorporation of a diverse functional groups. The advantages, such as simple and moderate conditions, excellent yields, and good functional group compatibility, may lead to application of this method for the synthesis of nitriles in the chemistry world.

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