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A practical one-pot conversion of alcohols into homologous nitriles catalyzed by PEG 400 and sodium iodide

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ABSTRACT

Alcohols were converted into nitriles by one-pot reactions with trimethylchlorosilane and sodium cyanide catalyzed by PEG400 and sodium iodide in dichloromethane in excellent yields.

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KEYWORDS

Alcohols;
Nitriles;
PEG400;
Trimethylchlorosilane;
Sodium cyanide;
Sodium iodide.

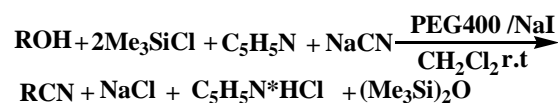
INTRODUCTION

Nitriles have played important roles in organic synthesis which can be converted into homologous carboxylic acids, esters, amides and amines^[1]. Literature survey indicates that there are a large number of methods reported for the preparation of this useful class of compounds^[2,3]. The classical methods for alcohols to nitriles proceed via sulphonates or halide intermediates which need two steps. An one-step procedure of alcohols into nitriles had been reported by Roman^[4]. But we found that it isn't suitable for the substrates which are sensitive to acids, and a quite amount of eliminated products formed for the secondary and tertiary alcohols in our application of this procedure because DMF and Acetonitrile have stronger polarity. Another deficiency is that DMF has higher boiling point, which is difficult on the separation with the products.

In recent years, polyethylene glycols (PEG) of various molecular weights have found much industrial application as PTC or solvent promoters in many organic

reactions since they can be regarded as acyclic crown ether analogues^[5,6]. With a medium molecular weight, PEG400 has been widely used as phase transfer catalysts in many organic reactions owing to their stability, low cost, and easy availability. Especially due to their liquid property and the two hydroxy groups, it has a more powerful ability to solubilise the inorganic salts in non-polar organic solvents such as benzene and dichloromethane. PEG400 was more suitable for solid-liquid phase^[7,8].

We wish to report a facile method for the one-step conversion of alcohols into nitriles catalyzed by PEG400 and sodium iodide in satisfactory yields with dichloromethane as solvent. The conversions of a series of alcohols into the corresponding nitriles by this method are shown in TABLE 1. The reaction is shown as follow:



It has been reported by the previous literature^[9] that trimethylchlorosilane can be recycled from $(\text{Me}_3\text{Si})_2\text{O}$ which is reclaimed with several different reagents such as SOCl_2 , PCl_5 , AlCl_3 , and HCl ^[10-13]. We used SOCl_2 as the reactant to reclaim trimethylchlorosilane with the yield of more than 85%.

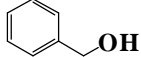
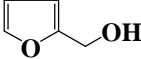
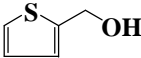
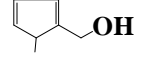
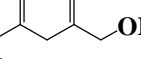
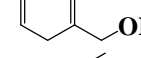
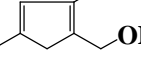
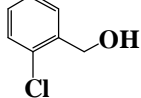
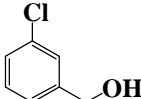
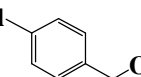
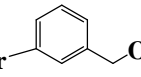
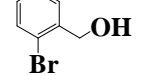
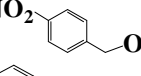
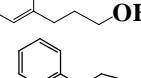
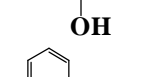
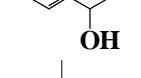
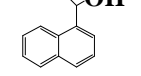
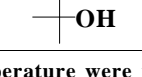
RESULTS AND DISCUSSION

Based on the results of the comparative experiments of several solvents with low boiling points, such as ethyl ether, dichloromethane, acetone and chloroform, we selected dichloromethane as solvent to ensure an excellent separation of the products from the mixture by distillation and good miscibility with PEG400. PEG400 as phase transfer catalyst allowed us to perform the condensation under mild condition in satisfactory yields and to separate the product mixture more easily. The appreciate amount of PEG400 was 3-5mol% to alcohols. A longer reaction time will be necessary with less PEG400 and the more products would be lost during the cause of washing with water if the more amount of PEG400 were employed^[14].

Compared with Roman's method, the amount of sodium cyanide has been reduced to 1.2equiv with pyridine as alkali to absorb hydrogen chloride which can reduce the generation of virulent hydrogen cyanide. In order to absorb hydrogen chloride, we compared with different kinds of bases, such as anhydrous sodium carbonate, magnesia and calcium oxide. Anhydrous sodium carbonate is a stronger inorganic base which can react with trimethylchlorosilane, it not only makes trimethylchlorosilane loss but also affect the absorption of hydrogen chloride. Pyridine is a weak organic alkali, It can absorb hydrogen chloride and be separated from the trimethylchlorosilane easily. So pyridine is a more suitable base.

As shown in the TABLE 1, primary and secondary alcohols are converted into the corresponding nitriles in excellent yields. The reaction was proceed by $\text{S}_{\text{N}}2$ process for different primary alcohols which are shown from entries (1) to (14), the arylmethanols have higher yields than other primary alcohols such as 3-Phenylpropyl alcohol in the entry (14) because arylmethanols have more reactive activity. The secondary alcohols as shown in the entries (15) to (17) can also proceed by $\text{S}_{\text{N}}2$ pro-

TABLE 1: Conversions of alcohols into nitriles

Entry	Alcohols	Time (h.)	Yield (%)	b.p./($^{\circ}\text{C}$ /mmHg)	
				Found	Reported ^[15]
1		4.5	92	102-104/10	234
2		5.5	85	60-64/6	58-61/5
3		4.5	85	113-118/20	115-120/22
4		5	91	111-114/10	244
5		5	89	108-111/10	240-241
6		5	90	112-115/10	242-243
7		5.5	88	125-128/10	128-130/13
8		4.5	94	109-112/10	240-242
9		5	90	135-137/10	134-136/10
10		4.5	93	125-128/5	265-267
11		4.5	91	136-138/10	140/13
12		5	92	114-116/5	114-115/5
13		4	92	115-117 (mp)	115-116(mp)
14		6	83	129-132/10	129-131/10
15 ^a		6.5	74	99-102/5	102-104/7
16 ^a		6.5	76	98-100/10	231
17 ^a		7	70	174-179/5	180-186/10
18		5	45	105-106	105-108

The temperature were processed at 40 $^{\circ}\text{C}$; ^aIced-water bath was used to lower the reaction temperature

cess because the carbonic ion is unstable in dichloro methane which has a lower polarity. We propose that the main reason for the low yields in entries (15) to (17)

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may be the side reaction of competitive elimination. In order to inhibit the side reaction, more solvent (1.5 times the amount) and an iced-water bath, to keep the temperature low, were used for the reactions in entries (15) to (17). They still give satisfied yields with a little longer reaction period. But the tertiary alcohol as shown in the entry (18) has a lower yield. We propose that the main reason for the low yield may be the reaction of competitive elimination. Longer reaction period was needed in the reactions for the products with high melting points. Higher yields could be obtained in the reactants with electron-withdrawing groups in the aromatic ring, such as -Cl, -Br, and -NO₂, than with electron-donating groups, such as -CH₃, mainly because the arylmethanols with electron-donating groups in the aromatic ring are more stable, it is more difficult in the reaction that the hydroxy was replaced by the cyanide ion.

The mechanism of the reaction is depicted in SCHEME 1. Without sodium iodide, longer reaction period was needed and the yields were reduced. So an active reagent Me₃SiI would be available for attack on the silyl ether to form the R-I with which would then react with the nucleophilic cyanide ion by S_N2 process. It is more suitable for the preparation of primary and secondary nitriles. Based on this, we propose that the reaction mechanism for the from entries 1 to 14 should be S_N2 type since the chloride anion is not a good leaving group, which might account for its longer reaction time and lower reaction rate.

In summary, an improved method for the conversion of alcohols into nitriles catalyzed by PEG400 and sodium iodide in satisfactory yields with dichloromethane as solvent is developed. The advantages of our method are inexpensive, practical and with the less pollution and ease of work-up.

EXPERIMENTAL

TLC was used to monitor the reaction process. TLC was GF₂₅₄ thin layer chromatography with petroleum ether/diethyl ether (2/1) used as eluent. Melting points were determined on a microscopy apparatus and uncorrected. ¹H-NMR spectra were obtained on a Bruker AVANCE (400MHz) spectrometer using TMS as internal standard and CDCl₃ as solvent. IR spectra were recorded on a Bio-Rad FTS-40 spectrometer

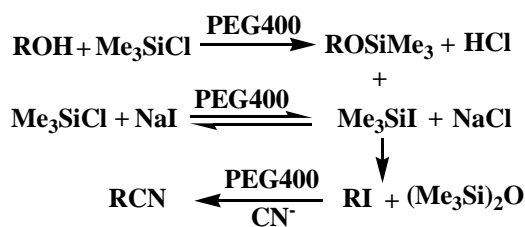
(KBr). All the liquid parent materials are fresh distilled. The products were also characterized by comparison of their Melting points and boiling points with the literature values. The reaction equipment was hermetical, nitrogen was used to eliminate the vapor before the addition of Me₃SiCl since its high activity to vapor.

General procedure for the preparation of 2-furonitrile from 2-furylcohol (entry 2)

A mixture of 2-furylcohol (4.32ml, 0.05mol), pyridine (6ml, 0.075mol), PEG400 (1ml, 5%), CH₂Cl₂ (30ml), NaCN (2.695g, 0.055mol), NaI (0.38g, 5%) was stirred in a 100ml three-necked, round-bottomed flask equipped with a magnetic bar, under nitrogen atmosphere, with the dropwise addition of Me₃SiCl (13.4ml, 0.105mol) over a period of about 2.0 hours. The mixture was heated in oil bath with stirring for 5.5 hours. The progress of the reaction was monitored by TLC. Upon completion, the solids were filtrated and meticulously washed with dried dichloromethane (5ml). The organic phase was washed with H₂O (3×10mL), dried with magnesium sulfate. After CH₂Cl₂ was recovered by distillation from the combined filtrate, 2-furonitrile 4.57g (85% yield) was collected at 60-64°C/BP₆ by distillation under reduced pressure. ¹H-NMR (CDCl₃): δ: 3.67 (s, 2H, CH₂), 6.13 (d 1H, CH), 7.11 (s, 1H, CH), 7.23 (d, 1H, CH)

General procedure for the preparation of 2-phenyl acetonitrile from phenylmethanol (entry 1):

A mixture of phenylmethanol (5.2ml, 0.05mol), pyridine (6ml, 0.075mol), PEG400 (1ml, 5%), CH₂Cl₂ (30ml), NaCN (2.695g, 0.055mol), NaI (0.38g, 5%) was stirred in a 100ml three-necked, round-bottomed flask equipped with a magnetic bar, under nitrogen atmosphere, with the dropwise addition of Me₃SiCl (13.4ml, 0.105mol) over a period of about 2.0 hours. The mixture was heated in oil bath with stirring for 4.5



SCHEME 1

hours. The progress of the reaction was monitored by TLC. Upon completion, the solids were filtrated and meticulously washed with dried dichloromethane (5ml). The organic phase was washed with H₂O(3×10mL), dried with magnesium sulfate. After CH₂Cl₂ was recovered by distillation from the combined filtrate, 2-phenylacetonitrile 5.34g (92% yield) was collected at 234°C by distillation. ¹H-NMR (CDCl₃): δ: 3.67 (s, 2H, CH₂), 7.06-7.14 (m, 5H, ArH) IR (KBr) ν: 3650, 3065, 3034, 2952, 2922, 2251, 1602, 1497, 1454, 1416, 1077, 1030, 940, 736, 697, 615cm⁻¹

The remaining nitriles were prepared in a similar manner. Further investigations into the utility of PEG400 and sodium iodide in generated reagent for synthetic transformations are continuing.

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