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Direct oxidative conversion of alkyl halides into nitriles with molecular iodine and 1,3-diiodo-5,5-dimethylhydantoin in aq ammonia

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ABSTRACT

Various benzylic halides were smoothly and directly converted into the corresponding aromatic nitriles in high yields using molecular iodine and 1,3-diiodo-5,5-dimethylhydantoin, respectively, in aq ammonia. Similarly, primary alkyl halides were also converted into corresponding nitriles in moderate to good yields using molecular iodine and 1,3-diiodo-5,5-dimethylhydantoin in aq ammonia, although a long reaction time was required. The present reaction is a new method for the preparation of aromatic nitriles from benzylic halides and a new method for the conversion of alkyl halides into corresponding nitriles with retention of the number of carbon atoms.

1. Introduction

Molecular iodine is one of the simplest oxidants currently available. It is highly affordable and has relatively low toxicity. Considered to be an environmentally benign oxidizing agent for organic synthesis, molecular iodine is used in various organic reactions, including the oxidation of alcohols or aldehydes to esters, the oxidation of sulfides to sulfoxides, the oxidation of cyclohexenones to benzene rings, the introduction of protecting groups, the deprotection of protecting groups, iodocyclization, carbon–carbon bond formation, and the formation of heterocycles.[1] Synthetic studies of 1,3-diiodo-5,5-dimethylhydantoin (DIH) are extremely limited,[2] although its structure is similar to that of *N*-iodosuccinimide (NIS). However, as DIH (MW=380) has two N–I bonds, it can be expected that 1 equiv of DIH has the same oxidative ability as 2 equiv of molecular iodine (MW=254) or NIS (MW=225). Thus, DIH is highly efficient and economical. On the other hand, nitriles are one of the most important synthetic transformation precursors because they can be easily converted into esters, amides, carboxylic acids, amines, and nitrogen-containing heterocycles, particularly tetrazoles that have potent biological activity,[3] and have been used as synthetic intermediates for agricultural chemicals, pharmaceuticals, and functional materials.[4] The most typical preparation method of nitriles is the reaction of alkyl halides with highly toxic metal cyanide via a nucleophilic pathway. However, this reaction induces one-carbon homologation. Consequently, nitriles are generally prepared by the dehydration of amides with $SOCl_2$, TsCl/Py, P_2O_5, $POCl_3$, $COCl_2$, $(EtO)_3P/I_2$, or Ph_3P/CCl_4, by the condensation of carboxylic acids with NH_3/silica gel or NH_3/ethyl polyphosphate, and by the reaction of esters with Me_2AlNH_2.[5] Nitriles can also be easily obtained by the oxidation of primary amines using AgO, $Pb(OAc)_4$, cobalt peroxide, $Na_2S_2O_8$ or $(Bu_4N)_2S_2O_8$ with metals, NaOCl, $K_3Fe(CN)_6$, Cu(I) or Cu(II) with oxygen, $RuCl_3$ or related Ru reagents, PhIO, and trichloroisocyanuric acid with TEMPO.[6] However, to the best of our knowledge, the direct oxidative conversion of alkyl halides into corresponding nitriles with retention of the number of carbon atoms has never been reported.[7] As part of our ongoing studies on the use of molecular iodine and DIH for organic synthesis,[8] we would like to report the direct oxidative conversion of benzylic halides and primary alkyl halides into corresponding aromatic nitriles and aliphatic nitriles with molecular iodine and DIH, respectively, in aq ammonia.

2. Results and discussion

2.1. Direct oxidative conversion of benzylic halides and alkyl halides into corresponding nitriles with molecular iodine in aq ammonia[7]

Recently, we reported the direct, efficient, practical, and less toxic oxidative conversion of primary alcohols and amines into

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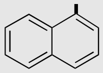
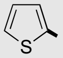
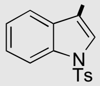
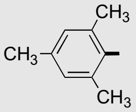
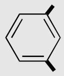
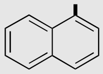
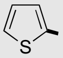
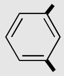
corresponding nitriles using molecular iodine in aq ammonia.[9] Based on the results of that study, we planned to perform the direct oxidative conversion of primary alkyl halides into corresponding nitriles using molecular iodine in aq ammonia. Primary alkyl halides should react with ammonia via the S_N2 nucleophilic pathway to form corresponding primary amines that can be smoothly oxidized to corresponding nitriles by molecular iodine in a one-pot manner. Practically, the reaction was carried out by treating benzyl chloride (1 mmol) with molecular iodine (2.1 mmol, 2.1 equiv) smoothly in aq ammonia (28–30%, 3 mL) at 60 °C in a standard reactor under an empty balloon to provide benzonitrile in good yield, as shown in Table 1 (entry 1). *p*-Chlorobenzyl, *p*-nitrobenzyl, *p*-methylbenzyl, *p*-methoxybenzyl, and 1-naphthylmethyl chlorides could be also converted into corresponding nitriles in good yields under the same conditions (entries 2–6). Benzyl, *p*-chlorobenzyl, *p*-nitrobenzyl, *p*-methylbenzyl, *p*-methoxybenzyl, and 1-naphthylmethyl bromides could be also converted into corresponding nitriles in good yields under the same conditions using 2.4 mmol of molecular iodine (entries 11–16). The same treatment of benzyl iodide provided benzonitrile in good yield (entry 19). 3-Chloromethyl-1-tosylindole and 2,4,6-trimethylbenzyl chloride could also be converted into corresponding nitriles in good yields under the same conditions (entries 8 and 9). When the same reaction was carried out with 2-halomethylthiophene as substrate, the yield of 2-cyanothiophene was low. However, after treating 2-halomethylthiophene with aq ammonia for 2 h at rt, adding molecular iodine to the reaction mixture, and warming the obtained mixture at 60 °C, 2-cyanothiophene was obtained in moderate yields (entries 7 and 17). One of the reasons why the yield of 2-cyanothiophene was lower than that of the other aromatic nitriles may be the low boiling point of 2-cyanothiophene. Treatment of 1,3-bis(chloromethyl)benzene and 1,3-bis(bromomethyl)benzene with molecular iodine (4.2 equiv and 4.8 equiv) in aq ammonia gave 1,3-dicyanobenzene in good yields (entries 10 and 18).

Clearly, the present reaction is a good method for the preparation of aromatic nitriles from benzylic halides directly. That means we do not need to use the Sandmeyer reaction of diazonium with toxic CuCN or the dehydration of aromatic amides with dehydrating agents.

When the same reaction was carried out under the same conditions with 1-iodododecane (1 mmol) as substrate, corresponding lauronitrile was not formed at all and the starting material was quantitatively recovered. Then, we examined the effect of additives as cosolvent, such as THF, dioxane, DMSO, or DMF, on promoting the nucleophilic reaction of ammonia with 1-iodododecane, and after several trials, we found that the addition of a small amount of DMF in a screw-capped glass vial (10 mL), instead of the use of a standard reactor under a balloon, improved the yield of lauronitrile. We believe that the evolution of ammonia gas from the reaction mixture under the present conditions is restrained by using a screw-capped glass vial, since the reaction of aliphatic primary alkyl halides with ammonia proceeds rather slowly compared with that of benzylic halides with ammonia. Thus, DMF (0.01 mL) was added to a mixture of 1-iodododecane in aq ammonia (1 mL) in a screw-capped glass vial, and the obtained mixture was warmed at 60 °C for 72 h. Then, molecular iodine (3 equiv) and aq ammonia (6 mL) were added to the reaction mixture and again the mixture was warmed at 60 °C for 4 h to provide lauronitrile in 75% yield (entry 1). Based on these results, 1-bromododecane and 1-chlorododecane were also treated with molecular iodine in aq ammonia and a small amount of DMF to form corresponding lauronitrile in good to moderate yields under the same conditions (entries 2 and 3). The reactivity depends on the alkyl halides, i.e., primary alkyl chlorides are less reactive than primary alkyl bromides and iodides. On the other hand, other primary alkyl-chain halides, such as 3-phenylpropyl halides, 4-phenylbutyl halides, 5-phenylpentyl halides, and 11-haloundecanoic acids, were efficiently converted into corresponding nitriles in good yields without DMF (entries 9–17). 1,10-Diiododecane and 1,10-dibromodecane provided the corresponding sebaconitrile in moderate yields by using 6 equiv of molecular iodine under the same conditions (entries 7 and 8). In contrast, cyclohexylmethyl halides were less reactive and adamantylmethyl halides did not react at all due to steric hindrance of the initial conversion into corresponding amines via the S_N2 reaction pathway with ammonia (entries 4–6) (Table 2).

Table 1
Conversion of benzylic halides into aromatic nitriles with I_2 in aq NH_3

$$\text{Ar−CH}_2\text{X} \xrightarrow[60\ °\text{C}]{\mathbf{I_2}\text{, aq.NH}_3\text{ (3.0 mL)}} \text{Ar−CN}$$

Entry	X	Ar	I_2 (equiv)	Time (h)	Yield[a] (%)
1	Cl	C_6H_5	2.1	4	73
2	Cl	*p*-ClC_6H_4	2.1	10	73
3	Cl	*p*-$O_2NC_6H_4$	2.1	4	92
4	Cl	*p*-$CH_3C_6H_4$	2.1	2	82
5	Cl	*p*-$CH_3OC_6H_4$	2.1	4	88
6	Cl		2.1	4	83
7	Cl		2.1	4[b]	60
8	Cl		2.1	4	61
9	Cl		2.1	4	86
10	Cl		4.2	4	81
11	Br	C_6H_5	2.4	4	78
12	Br	*p*-ClC_6H_4	2.4	8	78
13	Br	*p*-$O_2NC_6H_4$	2.4	4	88
14	Br	*p*-$CH_3C_6H_4$	2.4	4	88
15	Br	*p*-$CH_3OC_6H_4$	2.4	4	84
16	Br		2.4	4	87
17	Br		2.4	4[b]	49
18	Br		4.8	4	74
19	I	*p*-ClC_6H_4	2.4	8	78

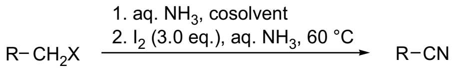
[a] Isolated yield.
[b] I_2 was added after 2 h.

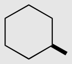
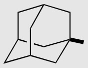
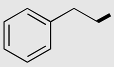
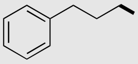
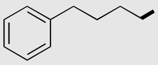
As a result, the present reaction is a novel means to convert alkyl halides into the corresponding nitriles, with retention of the number of carbon atoms.

2.2. Direct oxidative conversion of benzylic halides and alkyl halides into corresponding nitriles with DIH in aq ammonia

The use of 1,3-diiodo-3,3-dimethylhydantoin (DIH) in the iodination of aromatics was first reported in 1965.[2] However, to the best of our knowledge, it has been never used in organic synthesis. We have reported the direct, efficient, practical, and less toxic oxidative conversion of primary alcohols and amines into corresponding nitriles using DIH in aq ammonia.[9c] Thus, based on the

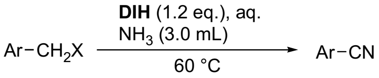
Table 2
Conversion of primary alkyl halides into aliphatic nitriles with I_2 in aq NH_3

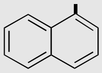
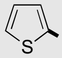
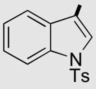
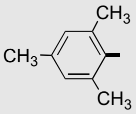
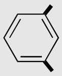
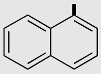
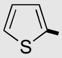
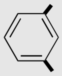


Entry	R	X	Cosolvent	First step			Second step		Yield[a] (%)
				aq NH_3 (mL)	Temp (°C)	Time (h)	aq NH_3 (mL)	Time (h)	
1[b]	$^{n}C_{11}H_{23}$–	I	DMF 0.01 mL	1.0	60	72	6.0	4	75
2[b]		Br	DMF 0.03 mL	1.0	60	72	6.0	4	69
3[b]		Cl	DMF 0.03 mL	1.0	100	72	6.0	4	49 (19[c])
4[b]		I	DMF 0.01 mL	1.0	100	24	6.0	4	48
5[b]		Br	DMF 0.01 mL	1.0	100	24	6.0	4	39 (7[c])
6[b]		I	DMF 0.01 mL	1.0	100	24	6.0	4	0 (99[c])
7[b,d]	–$(CH_2)_8$–	I	None	3.0	60	4	6.0	6	54
8[b,d]		Br	None	3.0	60	24	6.0	6	58
9[e]		I	None	3.0	60	12	3.0	4	70
10		Br	None	5.0	60	24	3.0	4	73
11[b]		Cl	None	3.0	100	24	3.0	4	65
12[b,e]		I	None	3.0	60	4	3.0	4	56
13		Br	None	5.0	60	48	3.0	4	68
14[b,e]		I	None	3.0	60	4	3.0	4	63
15[b]		Br	None	5.0	60	24	3.0	4	76
16	$HO_2C(CH_2)_9$–	I	None	3.0	60	4	3.0	4	53
17		Br	None	5.0	60	4	3.0	12	56

[a] Isolated yield.
[b] A screw-capped glass vail (10 mL) was used.
[c] Yield of the starting material.
[d] I_2 (6.0 equiv) was used.
[e] First step was carried out under dark condition.

Table 3
Conversion of benzylic halides into aromatic nitriles with DIH in aq NH_3



Entry	X	Ar	Time (h)	Yield[a] (%)
1	Cl	C_6H_5	4	73
2	Cl	p-ClC_6H_4	8	74
3	Cl	p-$O_2NC_6H_4$	4	84
4	Cl	p-$CH_3C_6H_4$	2	77
5	Cl	p-$CH_3OC_6H_4$	4	91
6	Cl		4	83
7	Cl		4[b]	50
8	Cl		4	60
9	Cl		4	53
10	Cl		4[c]	70
11	Br	C_6H_5	4	77
12	Br	p-ClC_6H_4	8	80
13	Br	p-$O_2NC_6H_4$	4	88
14	Br	p-$CH_3C_6H_4$	4	88
15	Br	p-$CH_3OC_6H_4$	4	85
16	Br		4	90
17	Br		4[b]	39
18	Br		4[c]	75
19	I	p-ClC_6H_4	8	82

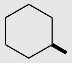
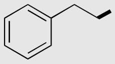
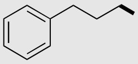
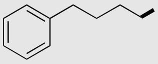
[a] Isolated yield.
[b] DIH was added after 2 h.
[c] DIH (2.4 equiv) was used.

above reactions of benzylic halides with molecular iodine in aq ammonia, benzyl chloride was treated with 1.2 equiv of DIH in aq ammonia (3 mL) for 4 h at 60 °C in a standard reactor under an empty balloon to provide benzonitrile in good yield, as shown in Table 3 (entry 1). Similar to the reactions with molecular iodine, p-chlorobenzyl, p-nitrobenzyl, p-methylbenzyl, p-methoxybenzyl, and 1-naphthylmethyl chlorides could be also converted into corresponding nitriles in good yields under the same conditions (entries 2–6). The reactivity of DIH is almost the same as that of molecular iodine. Benzyl, p-chlorobenzyl, p-nitrobenzyl, p-methylbenzyl, p-methoxybenzyl, and 1-naphthylmethyl bromides could be also converted into corresponding nitriles in good yields under the same conditions using 1.2 equiv of DIH (entries 11–16). The same treatment of benzyl iodide provided benzonitrile in good yield (entry 19). 3-Chloromethyl-1-tosylindole and 2,4,6-trimethylbenzyl chloride could be also converted into corresponding nitriles in moderate yields under the same conditions (entries 8 and

Table 4

Conversion of primary alkyl halides into aliphatic nitriles with DIH in aq NH_3

$$R{-}CH_2X \xrightarrow[\text{2. } \textbf{DIH} \text{ (2.0 eq.), aq. } NH_3\text{, 60 °C}]{\text{1. aq. } NH_3\text{, cosolvent}} R{-}CN$$

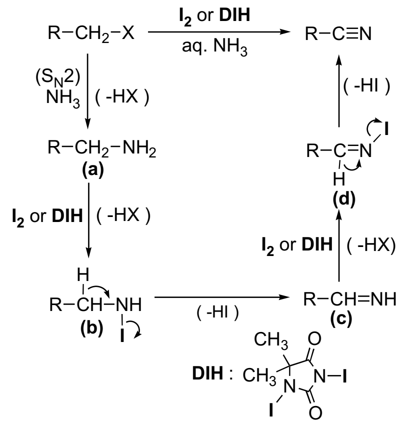
Entry	R	X	Cosolvent	First step			Second step		Yield[a] (%)
				aq NH_3 (mL)	Temp (°C)	Time (h)	aq NH_3 (mL)	Time (h)	
1[b]	$^{n}C_{11}H_{23}$–	I	DMF 0.01 mL	1.0	60	72	6.0	4	76
2[b]		Br	DMF 0.03 mL	1.0	60	72	6.0	4	69
3[b]		I	DMF 0.01 mL	1.0	100	24	6.0	4	43
4[b]		Br	DMF 0.03 mL	1.0	100	24	6.0	4	36
5[b,c]	–$(CH_2)_8$–	I	None	3.0	60	4	3.0	6	67
6[b,c]		Br	None	3.0	60	24	3.0	6	59
7[b,d]		I	None	3.0	60	12	3.0	4	74
8[b]		Br	None	3.0	60	24	3.0	4	72
9[b,d]		I	None	3.0	60	4	3.0	4	59
10[b]		Br	None	3.0	60	24	3.0	4	66
11[b,d]		I	None	3.0	60	4	3.0	4	60
12[b]		Br	None	3.0	60	24	3.0	4	64
13	$HO_2C(CH_2)_9$–	I	None	3.0	60	4	3.0	4	57
14		Br	None	3.0	60	4	3.0	12	56

[a] Isolated yield.

[b] A screw-capped glass vail (10 mL) was used.

[c] DIH (4 equiv) was used.

[d] First step was carried out under dark condition.



Scheme 1. Possible reaction pathway for nitrile.

9). The same treatment of 1,3-bis(chloromethyl)benzene and 1,3-bis(bromomethyl)benzene with DIH (2.4 equiv) in aq ammonia gave 1,3-dicyanobenzene in good yields (entries 10 and 18).

For primary alkyl iodides and bromides, the reaction did not proceed under the same conditions, similar to the case of molecular iodine. Thus, DMF (0.01 mL) was added to a mixture of 1-iodododecane in aq ammonia (1 mL) in a screw-capped glass vial, and the obtained mixture was warmed at 60 °C for 72 h. Then, DIH (2 equiv) and aq ammonia (6 mL) were added to the reaction mixture, and again the mixture was warmed at 60 °C for 4 h to provide lauronitrile in 76% yield as shown in Table 4 (entry 1). 1-Bromododecane was treated with DIH in aq ammonia and a small amount of DMF to form corresponding lauronitrile in good yield under the same conditions (entry 2). On the other hand, 3-phenylpropyl halides, 4-phenylbutyl halides, 5-phenylpentyl halides, and 11-haloundecanoic acids, were efficiently converted into corresponding nitriles in good yields without DMF (entries 7–14). The same treatment of 1,10-diiododecane and 1,10-dibromodecane provided the corresponding sebaconitrile in moderate to good yields by using 4 equiv of DIH under the same conditions (entries 5 and 6).

A possible reaction pathway for the conversion of benzylic halides and primary alkyl halides into corresponding aromatic nitriles and aliphatic nitriles, respectively, with molecular iodine and DIH in aq ammonia is shown in Scheme 1. The initial nucleophilic reaction of ammonia with benzylic or alkyl halide occurs to generate corresponding primary amine (a). N-Iodination of amine (a) with molecular iodine or DIH takes place to provide *N*-iodo compound (b), followed by β-elimination of HI with ammonia to provide aldemine (c). Then, aldemine (c) reacts with molecular iodine or DIH to generate *N*-iodo compound (d), and this is followed by β-elimination of HI with ammonia to give corresponding nitrile. NH_nI_{3-n} (n=2, 1, 0) formed by the reaction of ammonia with molecular iodine or DIH, may also work as effective N-iodonation species of amine and aldemine.

3. Conclusion

In conclusion, benzylic halides and primary alkyl halides could be easily and directly converted into corresponding aromatic nitriles and aliphatic nitriles, respectively, in good yields with retention of the number of carbon atoms, using molecular iodine and DIH in aq ammonia. The present reaction is not only a novel method for the preparation of aromatic nitriles from benzylic halides, but also a conversion method of primary alkyl halides into corresponding aliphatic nitriles, with retention of the number of carbon atoms. As is well known, the advantages of molecular iodine are operational simplicity, low cost, low toxicity, and availability, DIH is also a useful reagent because it is a pale yellow solid, has low toxicity, and does not sublimate like molecular iodine. Therefore, the present reactions should be a useful and environmentally benign method for the preparation of aromatic nitriles and aliphatic nitriles from benzylic halides and primary alkyl halides, respectively.

4. Experimental section

4.1. General

^{1}H NMR and ^{13}C NMR spectra were obtained with JEOL-JNM-GSX-400, JEOL-JNM-LA-400, and JEOL-JNM-LA-500 spectrometers.

Chemical shifts are expressed in parts per million downfield from TMS in δ units. Mass spectra were recorded on JEOL-HX-110 and JEOL-JMS-ATII15 spectrometers. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel 60 (Kanto Kagaku Co.) was used for column chromatography and Wakogel B-5F was used for preparative TLC.

4.2. Typical procedure for oxidative conversion of benzyl halides into nitriles with I_2

To a mixture of 4-methylbenzyl chloride (140.6 mg, 1 mmol) and aq NH_3 (3.0 mL, 45 mmol) was added I_2 (533.0 mg, 2.1 mmol) at rt under an empty balloon. The obtained mixture was stirred at 60 °C. After 4 h at the same temperature, the reaction mixture was quenched with H_2O (10 mL) and satd aq Na_2SO_3 (2 mL) at 0 °C, and was extracted with Et_2O (3×15 mL). The organic layer was washed with brine and dried over Na_2SO_4 to provide *p*-tolunitrile in 82% yield in an almost pure state. If necessary, the product was purified by column chromatography (silica gel; hexane/EtOAc=4:1) to give pure *p*-tolunitrile as a colorless solid; mp 25–26 °C. IR (NaCl): 2230 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.55 (2H, d, *J*=7.9 Hz), 7.27 (2H, d, *J*=7.9 Hz), 2.42 (3H, s).

4.3. Typical procedure for oxidative conversion of alkyl halides into nitriles with I_2

A mixture of 3-phenylpropyl bromide (199.1 mg, 1 mmol) and aq NH_3 (5.0 mL, 75 mmol) in a screw-capped glass vial (10 mL) was stirred at 60 °C for 24 h. Then, aq NH_3 (3.0 mL, 45 mmol) and I_2 (761.4 mg, 3.0 mmol) were added. After 4 h at the same temperature, the reaction mixture was quenched with H_2O (10 mL) and satd aq Na_2SO_3 (2 mL) at 0 °C, and was extracted with Et_2O (3×15 mL). The organic layer was washed with brine and dried over Na_2SO_4 to provide 3-phenylpropionitrile in 73% yield in an almost pure state. If necessary, the product was purified by column chromatography (silica gel; hexane/EtOAc=4:1) to give pure 3-phenylpropanenitrile as a colorless oil. IR (NaCl): 2250 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.34 (2H, t, *J*=8.2 Hz), 7.28 (1H, t, *J*=8.2 Hz), 7.23 (2H, d, *J*=8.2 Hz), 2.96 (2H, d, *J*=7.9 Hz), 2.62 (2H, d, *J*=7.9 Hz).

4.4. Typical procedure for oxidative conversion of benzyl halides into nitriles with DIH

To a mixture of 4-methylbenzyl chloride (140.6 mg, 1 mmol) and aq NH_3 (3.0 mL, 45 mmol) was added DIH (439.1 mg, 1.2 mmol) at rt under an empty balloon. The obtained mixture was stirred at 60 °C. After 4 h at the same temperature, the reaction mixture was quenched with H_2O (10 mL) and satd aq Na_2SO_3 (2 mL) at 0 °C, and was extracted with Et_2O (3×15 mL). The organic layer was washed with brine and dried over Na_2SO_4 to provide *p*-tolunitrile in 77% yield in an almost pure state. If necessary, the product was purified by column chromatography (silica gel; hexane/EtOAc=4:1) to give pure *p*-tolunitrile as a colorless solid; mp 25–26 °C. IR (NaCl): 2230 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.55 (2H, d, *J*=7.9 Hz), 7.27 (2H, d, *J*=7.9 Hz), 2.42 (3H, s).

4.5. Typical procedure for oxidative conversion of alkyl halides into nitriles with DIH

A mixture of 3-phenylpropyl bromide (199.1 mg, 1 mmol) and aq NH_3 (3.0 mL, 45 mmol) was stirred at 60 °C for 24 h in a screw-capped reactor, then to the mixture were added aq NH_3 (3.0 mL, 45 mmol) and DIH (731.9 mg, 2.0 mmol). After 4 h at the same temperature, the reaction mixture was quenched with H_2O (10 mL) and satd aq Na_2SO_3 (2 mL) at 0 °C, and was extracted with Et_2O (3×15 mL). The organic layer was washed with brine and dried over Na_2SO_4 to provide 3-phenylpropionitrile in 72% yield in an almost pure state. If necessary, the product was purified by column chromatography (silica gel; hexane/EtOAc=4:1) to give pure 3-phenylpropanenitrile as colorless oil. IR (NaCl): 2250 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.34 (2H, t, *J*=8.2 Hz), 7.28 (1H, t, *J*=8.2 Hz), 7.23 (2H, d, *J*=8.2 Hz), 2.96 (2H, d, *J*=7.9 Hz), 2.62 (2H, d, *J*=7.9 Hz).

All nitrile products mentioned in this work, except 10-cyanodecanoic acid and 1-(*p*-toluenesulfonyl)indole-3-carbonitrile, were identified by comparing with commercially available authentic samples.

4.5.1. *Benzonitrile*

Oil. IR (neat): 2230 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.67 (2H, d, *J*=7.7 Hz), 7.61 (1H, t, *J*=7.7 Hz), 7.48 (2H, t, *J*=7.7 Hz).

4.5.2. *4-Chlorobenzonitrile*

Mp 90–91 °C. IR (neat): 2225 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.61 (2H, d, *J*=8.5 Hz), 7.47 (2H, d, *J*=8.5 Hz).

4.5.3. *4-Methoxybenzonitrile*

Mp 55–57 °C. IR (neat): 2224 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.59 (2H, d, *J*=8.9 Hz), 6.96 (2H, d, *J*=8.9 Hz), 3.86 (3H, s).

4.5.4. *2-Cyanothiophene*

Oil. IR (neat): 2224 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.65 (1H, d, *J*=3.8 Hz), 7.62 (1H, d, *J*=5.0 Hz), 7.75 (1H, dd, *J*=5.0 and 3.8 Hz).

4.5.5. *1-Naphthonitrile*

Mp 34–35 °C. IR (neat): 2222 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=8.22 (1H, d, *J*=8.2 Hz), 8.06 (1H, d, *J*=8.2 Hz), 7.91 (1H, d, *J*=7.9 Hz), 7.89 (1H, d, *J*=7.9 Hz), 7.67 (1H, t, *J*=8.2 Hz), 7.60 (1H, t, *J*=8.2 Hz), 7.50 (1H, t, *J*=7.9 Hz).

4.5.6. *2,4,6-Trimethylbenzonitrile*

Mp 54–55 °C (lit.[10] mp 55 °C). IR (neat): 2220 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=6.93 (2H, s), 2.48 (6H, s), 2.32 (3H, s).

4.5.7. *Lauronitrile*

Oil. IR (neat): 2247 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=2.34 (2H, t, *J*=7.2 Hz), 1.66 (2H, quintet, *J*=7.2 Hz), 1.44 (2H, quintet, *J*=7.2 Hz), 1.35–1.25 (14H, br), 0.88 (3H, t, *J*=7.2 Hz).

4.5.8. *Cyclohexanecarbonitrile*

Oil. IR (neat): 2218 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=2.62 (1H, m), 1.85 (2H, m), 1.72 (4H, m), 1.55–1.37 (4H, m).

4.5.9. *1-Cyanoadamantane*

Mp 190–191 °C. IR (neat): 2229 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=2.04 (9H, br), 1.74 (6H, br).

4.5.10. *Sebaconitrile*

Oil. IR (neat): 2245 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=2.35 (4H, t, *J*=7.1 Hz), 1.66 (4H, quintet, *J*=7.1 Hz), 1.46 (4H, m), 1.35 (4H, m).

4.5.11. *1,3-Dicyanobenzene*

Mp 160–161 °C. IR (KBr): 2240 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=7.97 (1H, s), 7.92 (2H, d, *J*=8.1 Hz), 7.67 (1H, t, *J*=8.1 Hz).

4.5.12. *4-Nitrobenzonitrile*

Mp 140–142 °C. IR (neat): 2233 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=8.37 (2H, d, *J*=8.9 Hz), 7.90 (2H, d, *J*=8.9 Hz).

4.5.13. *4-Phenylbutanenitrile*

Oil. IR (neat): 2246 cm^{-1}. ^{1}H NMR ($CDCl_3$, TMS): δ=1.99 (2H, quintet, *J*=7.2 Hz), 2.32 (2H, t, *J*=7.2 Hz), 2.78 (2H, t, *J*=7.2 Hz), 7.18 (2H, d, *J*=7.3 Hz), 7.23 (1H, t, *J*=7.3 Hz), 7.32 (2H, t, *J*=7.3 Hz).

4.5.14. 5-Phenylpentanenitrile

Oil. IR (neat): 2246 cm^{-1}. ^{1}H NMR (CDCl$_3$, TMS): δ=1.74 (4H, m), 2.35 (2H, t, J=7.0 Hz), 2.66 (2H, t, J=7.5 Hz), 7.24 (5H, m).

4.5.15. 1-(p-Toluenesulfonyl)indole-3-carbonitrile

Mp 155–157 °C. IR (neat): 2231 cm^{-1}. ^{1}H NMR (CDCl$_3$, TMS): δ=8.11 (1H, s), 8.00 (1H, d, J=7.9 Hz), 7.83 (2H, d, J=8.4 Hz), 7.69 (1H, d, J=7.9 Hz), 7.44 (1H, t, J=7.9 Hz), 7.38 (1H, t, J=7.9 Hz), 7.31 (2H, d, J=8.4 Hz), 2.38 (3H, s). ^{13}C NMR (CDCl$_3$, TMS): δ=146.3, 133.9, 133.5, 133.1, 130.0, 128.2, 127.1, 126.4, 124.7, 120.2, 113.7, 113.4, 93.5, 21.6. HRMS: calcd for $C_{16}H_{13}O_2N_2S$: 297.0698; found: 297.0687.

4.5.16. 10-Cyanodecanoic acid

Mp 42–44 °C. IR (neat): 2243, 1690 cm^{-1}. ^{1}H NMR (CDCl$_3$, TMS): δ=2.35 (t, J=7.4 Hz, 2H), 7.34 (t, J=7.2 Hz, 1H), 1.64 (m, 4H), 1.44 (br, 2H) 1.32 (br, 9H). ^{13}C NMR (CDCl$_3$, TMS): δ=179.7, 119.9, 34.0, 29.1, 29.0, 28.72, 28.66, 25.4, 24.7, 17.2. HRMS: m/z calcd for $C_{11}H_{19}O_2N$: 198.1494; found: 198.1484.

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