

# Direct oxidative conversion of alcohols and amines to nitriles with molecular iodine and DIH in aq NH<sub>3</sub>

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**Abstract**—Simple and high-yield procedures for the direct oxidative conversion of various primary alcohols, and primary, secondary, and tertiary amines to the corresponding nitriles were successfully carried out with molecular iodine in aq ammonia and 1,3-diiodo-5,5-dimethylhydantoin in aq NH<sub>3</sub>, respectively.

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## 1. Introduction

Nitriles are one of the most important synthetic transformation precursors, especially into esters, amides, carboxylic acids, amines, and nitrogen-containing heterocycles.<sup>1</sup> Therefore, they have been used as synthetic intermediates for agricultural chemicals, pharmaceutical chemicals, and functional material chemicals.<sup>2</sup> The most typical synthetic method is the reaction of alkyl halides with very toxic metal cyanide via nucleophilic pathway, though one carbon is increased. Consequently, nitriles are generally prepared by the dehydration of amides with SOCl<sub>2</sub>, TsCl/Py, P<sub>2</sub>O<sub>5</sub>, POCl<sub>3</sub>, COCl<sub>2</sub>, (EtO)<sub>3</sub>P/I<sub>2</sub>, Ph<sub>3</sub>P/CCL<sub>4</sub>, etc., by the condensation of carboxylic acids with NH<sub>3</sub>/silica gel, NH<sub>3</sub>/ethyl polyphosphate, etc., and by the reaction of esters with Me<sub>2</sub>AlNH<sub>2</sub>.<sup>3</sup> On the other hand, oxidative conversion of primary amines to the corresponding nitriles has been well studied using AgO,<sup>4a</sup> Pb(OAc)<sub>4</sub>,<sup>4b–4c</sup> cobalt peroxide,<sup>4f</sup> Na<sub>2</sub>S<sub>2</sub>O<sub>8</sub> or (Bu<sub>4</sub>N)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> with metals,<sup>4g–4j</sup> NaOCl,<sup>4k–4m</sup> K<sub>3</sub>Fe(CN)<sub>6</sub>,<sup>4n</sup> Cu(I) or Cu(II) with oxygen,<sup>4o–4r</sup> RuCl<sub>3</sub> and related Ru reagents,<sup>4s–4w</sup> PhIO,<sup>4x</sup> and trichloroisocyanuric acid with TEMPO.<sup>4y</sup> Here, as a part of our study for the synthetic use of molecular iodine and related reagents for organic synthesis,<sup>5</sup> we would like to report for the direct oxidative conversion of primary alcohols, and primary, secondary, and tertiary amines to the corresponding nitriles with molecular iodine and related reagents.

## 2. Results and discussion

### 2.1. Conversion of primary alcohols, and primary, secondary, and tertiary amines to nitriles with molecular iodine in aq NH<sub>3</sub>

Molecular iodine is a mild, cheap, and easily available oxidizing reagent, and it is useful because it is solid form and is less toxic than other halogens such as molecular bromine and chlorine. Previously, simple conversion of aldehydes to the corresponding nitriles using molecular iodine in aq NH<sub>3</sub> and CH<sub>3</sub>OH or THF was reported.<sup>6</sup> Today, to the best of our knowledge, direct oxidative conversion of alcohol to the corresponding nitriles in one-pot manner is extremely limited, i.e. using NiSO<sub>4</sub> and K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> in aq NaOH,<sup>7a</sup> NH<sub>4</sub>HCO<sub>3</sub>, (Bu<sub>4</sub>N)<sub>2</sub>S<sub>2</sub>O<sub>8</sub>, and a catalytic amount of Cu(HCO<sub>2</sub>)<sub>2</sub>·Ni(HCO<sub>2</sub>)<sub>2</sub> in aq KOH and <sup>i</sup>PrOH,<sup>7b</sup> and MnO<sub>2</sub>, NH<sub>3</sub>, and MgSO<sub>4</sub> in THF and <sup>i</sup>PrOH for benzylic and cinnamic alcohols.<sup>7c</sup>

At first, a direct, efficient, practical, and less toxic oxidative conversion of primary alcohols to the corresponding nitriles, using molecular iodine in aq NH<sub>3</sub> was studied.<sup>8</sup> Thus, when 3-phenylpropanol (1 mmol) was treated with molecular iodine in aq NH<sub>3</sub>, changing the amounts of molecular iodine and aq NH<sub>3</sub> under empty balloon, 3-phenylpropionitrile was formed as shown in Table 1. When the reaction was carried out in a sealed tube, the amount of aq NH<sub>3</sub> could be reduced (entries 7–10). However, it is not so practical. The results indicate that the reaction with 3.0 equiv of molecular iodine and 45 equiv of aq NH<sub>3</sub> (3 mL, 28–30%) under empty balloon at 60 °C gave 3-phenylpropionitrile in the best yield (entry 5).

**Keywords:** Primary alcohol; Primary amine; Secondary amine; Tertiary amine; Iodine; 1,3-Diiodo-5,5-dimethylhydantoin; Nitrile; Aq NH<sub>3</sub>.

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**Table 1.** Oxidative conversion of 3-phenylpropanol to 3-phenylpropionitrile with I<sub>2</sub>/aq NH<sub>3</sub>

$$\text{Ph}(\text{CH}_2)_2\text{CH}_2\text{OH} \xrightarrow[24\text{h}]{\text{I}_2, \text{aq. NH}_3} \text{Ph}(\text{CH}_2)_2\text{CN}$$

Entry	I <sub>2</sub> /aq NH <sub>3</sub> (equiv)	Temp. (°C)	Yield (%)
1	2.5/10	rt	14 (86 <sup>a</sup> )
2	2.5/10	50	62 (28 <sup>a</sup> )
3	2.5/20	50	74 (20 <sup>a</sup> )
4	2.5/45	50	67 (29 <sup>a</sup> )
5	3.0/45	60	91
6 <sup>b</sup>	3.0/10	60	51 (34 <sup>a</sup> )
7 <sup>c</sup>	3.0/5	60	31 (53 <sup>a</sup> )
8 <sup>c</sup>	3.0/10	60	48 (31 <sup>a</sup> )
9 <sup>c</sup>	3.0/15	60	81 (12 <sup>a</sup> )
10 <sup>c</sup>	3.0/20	60	85 (12 <sup>a</sup> )

<sup>a</sup> Yield of the starting material.<sup>b</sup> K<sub>2</sub>CO<sub>3</sub> (2.0 equiv) was added.<sup>c</sup> Reaction was carried out in a sealed tube.

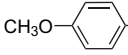
When the reactivity of molecular iodine was compared with those of *N*-bromosuccinimide (NBS), *N*-chlorosuccinimide (NCS), *N*-iodosuccinimide (NIS), ICl, and Ca(OCl)<sub>2</sub> in aq NH<sub>3</sub> using *p*-methoxybenzyl alcohol and 1-dodecanol, NBS and NCS did not work, and NIS and ICl gave the corresponding nitriles in good to moderate yields as shown in Table 2. However, the yields with molecular iodine were better than those with NIS and ICl, and practically NIS is expensive and ICl is not so easy to operate. Based on these results, various primary alcohols such as benzylic alcohols, straight-chained alcohols, adamantylmethanol were treated with molecular iodine in aq NH<sub>3</sub> to provide the corresponding nitriles in good yields, except for cinnamyl alcohol, which induced further addition reaction to the formed cinnamionitrile by ammonia in aq NH<sub>3</sub> under the warming temperature as shown in Table 3. The reaction could be also carried out in preparative scale without any problem to give the corresponding nitrile in good yield (entry 15). Diols could be also transformed to the corresponding dinitriles using twice the amount of molecular iodine and aq NH<sub>3</sub> (entries 13 and 20).

Today, some outline work on the reaction of benzylamine with molecular iodine in acetonitrile to form imine, *N*-benzylidenebenzylamine, benzonitrile, etc., was reported.<sup>9</sup>

However, detailed study for the reaction of amines with molecular iodine in aq NH<sub>3</sub> has not been carried out. Thus,


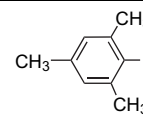
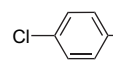
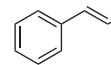
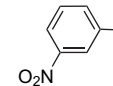


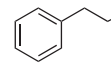
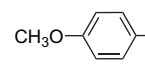
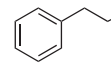
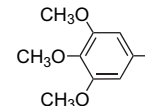
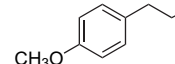

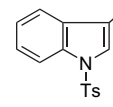

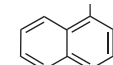

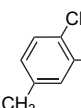
**Table 2.** Oxidative conversion of alcohols to nitriles with halogen reagents in aq NH<sub>3</sub>

$$\text{R-CH}_2\text{OH} \xrightarrow[60\text{ }^\circ\text{C}]{\text{Reagent, aq. NH}_3 (3.0\text{ mL})} \text{R-CN}$$

Entry	R-	Reagent	Time (h)	Yield (%)
1		I <sub>2</sub> (3.0 equiv)	2	99
2		NBS (3.0 equiv)	2	2 (88 <sup>a</sup> )
3		NCS (3.0 equiv)	2	0 (99 <sup>a</sup> )
4		NIS (3.0 equiv)	2	92 (8 <sup>b</sup> )
5		ICI (3–6 equiv)	2	97
6		Ca(OCl) <sub>2</sub> (1.5 equiv)	2	0 (94 <sup>a</sup> )
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> -	I <sub>2</sub> (3.0 equiv)	8	91
8		NIS (3.0 equiv)	8	60 (40 <sup>a</sup> )
9		ICI (3–6 equiv)	8	67 (31 <sup>a</sup> )

<sup>a</sup> Yield of the starting material.**Table 3.** Oxidative conversion of alcohol to nitriles with I<sub>2</sub>/aq NH<sub>3</sub>

$$\text{R-CH}_2\text{OH} \xrightarrow[60\text{ }^\circ\text{C}]{\text{I}_2 (3.0\text{ eq.}) / \text{aq. NH}_3 (3.0\text{ mL})} \text{R-CN}$$

Entry	R-	Time (h)	Yield (%)	Entry	R-	Time (h)	Yield (%)
1		2	86	11 <sup>a</sup>		30	68
2		2	95	12		4	42
3		3	92	13 <sup>b</sup>		2	99
4		3	77	14		24	91
5		2	99	15 <sup>c</sup>		42	90
6		2	97	16		21	63
7		3	67	17	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>11</sub> -	8	91
8		4	66	18		8	68
9		4	80	19		6	90
10		6	80	20 <sup>b</sup>	-(CH <sub>2</sub> ) <sub>8</sub> -	24	99
















<sup>a</sup> Reaction was carried out at 80 °C and I<sub>2</sub> (1.5 equiv) was added again after 24 h.<sup>b</sup> I<sub>2</sub> (6.0 equiv) and aq NH<sub>3</sub> (6.0 mL) were used.<sup>c</sup> Reaction was carried out using 10 mmol (1.36 g) of alcohol.

the reaction was very simply carried out by treatment of benzylic and aliphatic primary amines (1 mmol) with molecular iodine (2.1–3.0 mmol) in aq NH<sub>3</sub> (28–30%, 3 mL) at 60 °C to provide the corresponding nitriles in good yields as shown in Table 4.<sup>10</sup> When the same reaction was carried out in water or <sup>t</sup>BuOH in the presence of K<sub>2</sub>CO<sub>3</sub>, instead of aq ammonia, the yield of nitrile was decreased as shown in entries 5 and 6. Diamines were also converted to the corresponding dinitriles in good yields (entries 14–17). DL-2-phenylglycine was converted to benzonitrile through oxidative decarboxylation (entries 18 and 19).

When *N*-methyl secondary amines and *N,N*-dimethyl tertiary amines were treated with molecular iodine under the same conditions, the corresponding nitriles could be again obtained in good yields as shown in Table 5. Moreover, bis(dodecyl)amine (1 mmol), bis(4-methylbenzyl)amine (1 mmol), tris(dodecyl)amine (1 mmol), and tris(4-methylbenzyl)amine (1 mmol) were treated with 4.5 equiv, 4.5 equiv, 6.5 equiv, and 6.5 equiv of molecular iodine, in

**Table 4.** Oxidative conversion of primary amines to nitriles with I<sub>2</sub>/aq NH<sub>3</sub>

$$\text{R-CH}_2\text{NH}_2 \xrightarrow[60^\circ\text{C}]{\text{I}_2, \text{aq. NH}_3 (3.0 \text{ mL})} \text{R-CN}$$

Entry	R-	I <sub>2</sub> (equiv)	Time (h)	Yield (%)
1		2.1	1	56
2		3.0	1	68
3		2.1	2	80
4		3.0	2	81
5		3.0 <sup>a</sup>	2	30
6		3.0 <sup>b</sup>	8	50 (20 <sup>c</sup> )
7		2.1	2	78
8		3.0	2	87
9		2.1	1	77
10		3.0	1	82
11	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> -	2.1	4	75
12	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> -	3.0	4	83
13		3.0	2	72
14 <sup>d</sup>		4.2	2	79
15 <sup>d</sup>		6.0	2	90
16 <sup>d</sup>	-(CH <sub>2</sub> ) <sub>8</sub> -	4.2	4	61
17 <sup>d</sup>	-(CH <sub>2</sub> ) <sub>8</sub> -	6.0	4	61
18		2.1	1	80 <sup>e</sup>
19		3.0	1	95 <sup>e</sup>

<sup>a</sup> H<sub>2</sub>O (3.0 mL) and K<sub>2</sub>CO<sub>3</sub> (3.0 equiv) were used instead of aq NH<sub>3</sub>.<sup>b</sup> *t*-BuOH (3.0 mL) and K<sub>2</sub>CO<sub>3</sub> (3.0 equiv) were used instead of aq NH<sub>3</sub>.<sup>c</sup> Yield of the starting material.<sup>d</sup> Double amount of aq NH<sub>3</sub> was used.<sup>e</sup> Product was benzonitrile.

aq NH<sub>3</sub> under the same conditions to give the corresponding laurionitrile (1.67 mmol), *p*-tolunitrile (1.82 mmol), laurionitrile (2.14 mmol), and *p*-tolunitrile (2.53 mmol) in 84%, 91%, 71%, and 83% yields, respectively (entries 17–20).















## 2.2. Conversion of primary alcohols, and primary, secondary, and tertiary amines to nitriles with DIH in aq NH<sub>3</sub>

1,3-Diiodo-5,5-dimethylhydantoin (DIH) was also studied as another direct, efficient, practical, and less toxic oxidative reagent for the conversion of primary alcohols to the corresponding nitriles in aq NH<sub>3</sub>. Today, to the best of our knowledge, synthetic use of DIH is extremely limited, while the iodination of aromatics with DIH has been reported.<sup>11</sup>

Thus, the reaction was very simply carried out by treatment of 1-dodecanol (1 mmol) and 1-dodecylamine (1 mmol) with DIH (2.0 mmol for 1-dodecanol and 1.2 mmol for 1-dodecylamine) in aq NH<sub>3</sub> (28–30%, 3 mL) at 60 °C under dark conditions to provide the corresponding laurionitrile in 97% and 88% yields, respectively, as shown in Table 6 (entries 1 and 5).<sup>12</sup> When the same reaction was carried out with NIS (4.0 mmol for 1-dodecanol and 2.4 mmol for 1-dodecylamine) in aq NH<sub>3</sub>, laurionitrile was also obtained (entries 2 and 6). However, the yields tend to decrease as compared with DIH. On the other hand, NCS and NBS did not provide the corresponding laurionitrile at all, and the starting materials remained mainly (entries 3, 4, 7, and 8).

**Table 5.** Oxidative conversion of secondary and tertiary amines to nitriles with I<sub>2</sub>/aq NH<sub>3</sub>

$$\text{R-CH}_2\text{X} \xrightarrow[60^\circ\text{C}]{\text{I}_2, \text{aq. NH}_3 (3 \text{ mL})} \text{R-CN}$$

Entry	R-	X	I <sub>2</sub> (equiv)	Time (h)	Yield (%)
1		NH(CH <sub>3</sub> )	2.1	4	49
2		NH(CH <sub>3</sub> )	3.5	4	71
3		NH(CH <sub>3</sub> )	4.0	4	71
4		N(CH <sub>3</sub> ) <sub>2</sub>	2.1	0.5	41
5		N(CH <sub>3</sub> ) <sub>2</sub>	3.5	0.5	71
6		N(CH <sub>3</sub> ) <sub>2</sub>	4.0	0.5	74
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> -	NH(CH <sub>3</sub> )	3.5	4	76
8	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> -	N(CH <sub>3</sub> ) <sub>2</sub>	3.5	0.5	73
9		NH(CH <sub>3</sub> )	3.5	1	81
10		N(CH <sub>3</sub> ) <sub>2</sub>	4.0	1	67
11		NH(CH <sub>3</sub> )	3.5	1	84
12		N(CH <sub>3</sub> ) <sub>2</sub>	4.0	1	77
13		NH(CH <sub>3</sub> )	3.5	2	77
14		N(CH <sub>3</sub> ) <sub>2</sub>	5.0	2	72
15		NH(CH <sub>3</sub> )	3.5	2	96
16		N(CH <sub>3</sub> ) <sub>2</sub>	5.0	6	76
17	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> -	NH(CH <sub>2</sub> R)	4.5	4	84
18 <sup>a</sup>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> -	N(CH <sub>2</sub> R) <sub>2</sub>	6.5	6	71
19		NH(CH <sub>2</sub> R)	4.5	8	91
20		N(CH <sub>2</sub> R) <sub>2</sub>	6.5	4	83

<sup>a</sup> Aq NH<sub>3</sub> (9 mL) was used.**Table 6.** Oxidative conversion of 1-dodecanol and 1-dodecylamine with DIH in aq NH<sub>3</sub>

$$\text{C}_{11}\text{H}_{23}\text{-CH}_2\text{X} \xrightarrow[60^\circ\text{C, dark}]{\text{Reagent, aq. NH}_3 (3.0 \text{ mL})} \text{C}_{11}\text{H}_{23}\text{-CN}$$

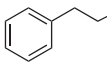
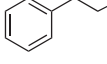
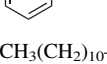


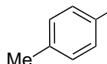
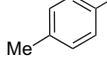
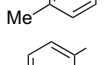
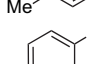
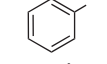
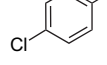
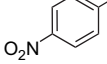
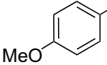


Entry	X	Reagent	Equiv	Time (h)	Yield (%)
1	OH	DIH	2.0	32	97
2	OH	NIS	4.0	32	65 (16 <sup>a</sup> )
3	OH	NBS	4.0	32	0 (99 <sup>a</sup> )
4	OH	NCS	4.0	32	0 (99 <sup>a</sup> )
5	NH <sub>2</sub>	DIH	1.2	6	88
6	NH <sub>2</sub>	NIS	2.4	6	71
7	NH <sub>2</sub>	NBS	2.4	6	0 (57 <sup>a</sup> )
8	NH <sub>2</sub>	NCS	2.4	6	0 (51 <sup>a</sup> )

<sup>a</sup> Yield of the starting material.

Based on these results, various primary alcohols and primary amines were treated with DIH in aq NH<sub>3</sub> to form the corresponding nitriles in good yields (Tables 7 and 8). The reactivity depends on the alcohols used, thus benzylic alcohols were smoothly converted to the corresponding nitriles in good yields, using 1.5 equiv of DIH (entries 8–16 in Table 7), while aliphatic primary alcohols required 2.0 equiv of DIH and long reaction time (entries 1–6 in Table 7). The same treatment of 1,8-octanediol and *p*-xylene glycol provided the corresponding dinitriles in good yields, respectively (entries 7 and 17 in Table 7). The reaction could be also carried out in preparative scale without any problem to provide the corresponding nitrile in good yield (entry 5 in Table 7). Secondary and tertiary amines were also converted to the corresponding nitriles in good yields (entries

**Table 7.** Oxidative conversion of alcohols to nitriles with DIH/aq NH<sub>3</sub>

$$\text{R-CH}_2\text{OH} \xrightarrow[60^\circ\text{C, dark}]{\text{DIH, aq. NH}_3 (3.0\text{ mL})} \text{R-CN}$$

Entry	R–	DIH (equiv)	Time (h)	Yield (%)
1 <sup>a</sup>		1.5	24	63
2		1.5	24	69
3		2.0	24	77
4	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	2.0	32	97
5 <sup>b</sup>		2.0	32	95
6		2.0	32	82
7 <sup>c</sup>	–(CH <sub>2</sub> ) <sub>6</sub> –	4.0	24	94
8		1.1	3	66
9		1.3	3	77
10		1.5	3	84
11		1.7	3	83
12		1.5	5	71
13		1.5	3	81
14		1.5	12	89
15		1.5	3	91
16		1.5	8	92
17		3.0	4	95








<sup>a</sup> Flask was not covered with Alumi-foil.<sup>b</sup> Reaction was carried out using 10 mmol of alcohol.<sup>c</sup> Double amount of aq NH<sub>3</sub> was used.

11–18 in Table 8). Today, it is known that aldehydes smoothly react with molecular iodine in aq NH<sub>3</sub> to provide the corresponding nitriles.<sup>6</sup> DIH also reacts with aldehydes including cinnamaldehyde in aq NH<sub>3</sub> at room temperature to provide the corresponding nitriles in good yields as shown in Table 9.

Treatment of imines, which were prepared from the corresponding aldehydes with primary amines, with molecular iodine and DIH in aq NH<sub>3</sub> at 60 °C gave the corresponding nitriles, respectively, in good yields as shown in Table 10. Based on these results, a plausible reaction pathway for the conversion of primary alcohol and primary amine to the corresponding nitrile with molecular iodine and DIH is shown in Scheme 1. Thus, the initial O-iodination and N-iodination of alcohol and amine with molecular iodine and DIH occurred to form O-iodo and N-iodo compounds (**a**), respectively, followed by β-elimination of HI by NH<sub>3</sub> to form aldehyde and aldimine (**b**), respectively. Here aldehyde smoothly reacts with NH<sub>3</sub> to form aldimine (**c**). Then, aldimine (**c**) reacts with molecular iodine and DIH in the presence of NH<sub>3</sub> to form N-iodo aldimine (**d**), followed by β-elimination of HI by NH<sub>3</sub> to generate the corresponding nitrile. Practically, aldehydes react with molecular iodine and DIH smoothly at room temperature in aq NH<sub>3</sub> to provide the corresponding nitriles in good yields. Imines also react

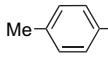
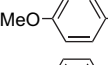
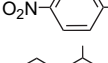



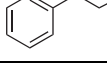
**Table 8.** Oxidative conversion of amines to nitriles with DIH/aq NH<sub>3</sub>

$$\text{R-CH}_2\text{NX} \xrightarrow[60^\circ\text{C, dark}]{\text{DIH, aq. NH}_3 (3.0\text{ mL})} \text{R-CN}$$

Entry	R–	NX	DIH (equiv)	Time (h)	Yield (%)
1	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	NH <sub>2</sub>	1.1	4	84
2		NH <sub>2</sub>	1.2	4	85
3		NH <sub>2</sub>	1.2	6	88
4		NH <sub>2</sub>	1.5	4	88
5		NH <sub>2</sub>	1.2	2	79
6		NH <sub>2</sub>	1.2	2	92
7		NH <sub>2</sub>	1.2	3	72
8		NH <sub>2</sub>	1.2	4	93
9		NH <sub>2</sub>	1.2	4	98
10	–(CH <sub>2</sub> ) <sub>8</sub> –	NH <sub>2</sub>	2.4 <sup>a</sup>	6	65
11	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	NH(CH <sub>3</sub> )	1.7	6	76
12		N(CH <sub>3</sub> ) <sub>2</sub>	1.7 <sup>a</sup>	0.5	80
13		NH(CH <sub>3</sub> )	1.7	3	79
14		N(CH <sub>3</sub> ) <sub>2</sub>	2.5 <sup>a</sup>	2	72
15	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	NH(CH <sub>2</sub> R)	2.4	10	84
16		N(CH <sub>2</sub> R) <sub>2</sub>	3.6 <sup>b</sup>	6	84
17		NH(CH <sub>2</sub> R)	2.4	6	84
18		N(CH <sub>2</sub> R) <sub>2</sub>	4.2 <sup>c</sup>	48	85

<sup>a</sup> Aq NH<sub>3</sub> (6 mL) was used.<sup>b</sup> Aq NH<sub>3</sub> (9 mL) was used.<sup>c</sup> Aq NH<sub>3</sub> (3 mL) was added again after 24 h.**Table 9.** Oxidative conversion of aldehydes to nitriles with DIH/aq NH<sub>3</sub>

$$\text{R-CHO} \xrightarrow[\text{r.t.}]{\text{DIH (0.6 equiv.) aq. NH}_3 (3.0\text{ mL})} \text{R-CN}$$

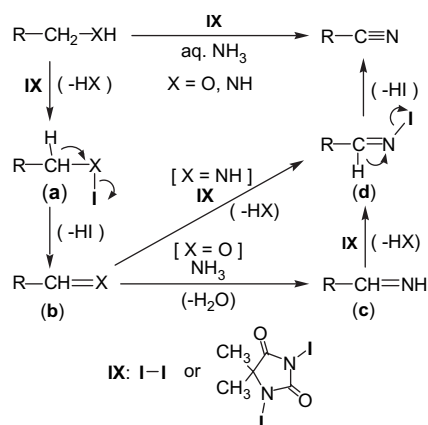
Entry	R–	Time (h)	Yield (%)
1		1	89
2		1	90
3		2	78
4		2	94
5 <sup>a</sup>		3	73
6		1	88
7 <sup>b</sup>		1	77

<sup>a</sup> DIH (1.2 equiv) and aq NH<sub>3</sub> (6.0 mL) were used.<sup>b</sup> THF (1 mL) was used and reaction was carried out at 0 °C.

**Table 10.** Oxidative conversion of imines to nitriles with DIH/aq NH<sub>3</sub>

Entry	R–	R'–	Reagent	Time (h)	Yields (%)	
					R–CN	R'–CN
1		CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	I <sub>2</sub> (4.0 equiv)	16	79	80
2		CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	DIH (2.0 equiv)	6	79	75
3			I <sub>2</sub> (4.0 equiv)	16	79	72
4			DIH (2.0 equiv)	3	94	79
5		CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	I <sub>2</sub> (4.0 equiv)	16	95	81
6		CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> –	DIH (2.0 equiv)	10	94	72
7			I <sub>2</sub> (4.0 equiv)	16	96	70
8			DIH (2.0 equiv)	4	97	80

with molecular iodine and DIH in aq NH<sub>3</sub> at 60 °C to form the corresponding nitriles in good yields.

**Scheme 1.** Plausible reaction pathway for nitrile.

### 3. Conclusion

In summary, primary alcohols, and primary, secondary, and tertiary amines could be easily and efficiently converted to the corresponding nitriles in good yields, using molecular iodine and DIH in aq NH<sub>3</sub>. As is well known, the advantages of molecular iodine are operational simplicity, low cost, and low toxicity. DIH can be also used for the same oxidative conversion of primary alcohols, and primary, secondary, and tertiary amines to the corresponding nitriles in good yields. DIH is a pale yellow solid and does not sublime, like molecular iodine. So it is more convenient to operate the reaction with DIH.

## 4. Experimental section

### 4.1. General

<sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained with JEOL-JNM-LA-400, JEOL-JNM-LA-400s, JEOL-JNM-LA-500 spectrometers. Chemical shifts are expressed in parts per million

downfield from tetramethylsilane (TMS) in  $\delta$  units. Mass spectra were recorded on JEOL-HX-110 and JEOL-JMS-AT115 spectrometers. Melting points were determined on 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.

Most of the nitriles mentioned in this work were identified with commercially available authentic samples, except for 1-(*p*-toluenesulfonyl)indole-3-carbonitrile and 3-(*p*-toluenesulfonyl)aminomethylbenzonitrile.

### 4.2. Typical procedure for oxidative conversion of primary alcohols to nitriles with I<sub>2</sub>

To a mixture of 3-phenylpropanol (136.2 mg, 1 mmol) and aq NH<sub>3</sub> (3 mL, 45 mmol) was added I<sub>2</sub> (761 mg, 3 mmol) at room temperature under empty balloon. Empty balloon was used to reduce the escape of ammonia gas from the reaction mixture. The mixture obtained was stirred at 60 °C. After 24 h at the same temperature, the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (3 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×20 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide 3-phenylpropionitrile in 91% yield in an almost pure state. If necessary, the product was purified by flash column chromatography on silica gel (hexane/EtOAc=4:1) to give pure 3-phenylpropionitrile as a colorless oil. IR (NaCl): 2250 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$ =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, t, *J*=7.4 Hz), 2.62 (2H, t, *J*=7.4 Hz).

### 4.3. Typical procedure for oxidative conversion of primary amines to nitriles with I<sub>2</sub>

To a mixture of 4-methylbenzylamine (121.2 mg, 1 mmol) and aq NH<sub>3</sub> (3.0 mL, 45 mmol) was added I<sub>2</sub> (533.0 mg, 2.1 mmol) at room temperature under an empty balloon. The resulting mixture was stirred at 60 °C. After 2 h at the same temperature, the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (3 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×15 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide *p*-tolunitrile in 80% 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 °C. IR (NaCl): 2230 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$ =7.55 (2H, d, *J*=7.9 Hz), 7.27 (2H, d, *J*=7.9 Hz), 2.42 (3H, s).

### 4.4. Typical procedure for oxidative conversion of tertiary amines to nitriles with I<sub>2</sub>

To a mixture of *N,N*-dimethyl-3-phenylpropylamine (163.2 mg, 1 mmol) and aq NH<sub>3</sub> (3.0 mL, 45 mmol) was added I<sub>2</sub> (888.3 mg, 3.5 mmol) at room temperature under an empty balloon. The resulting mixture was stirred at 60 °C. After 0.5 h at the same temperature, the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (3 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×15 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide 3-phenylpropionitrile in



71% yield in an almost pure state. If necessary, the product was purified by column chromatography on silica gel (hexane/EtOAc=4:1) to give pure 3-phenylpropionitrile as a colorless oil.

#### 4.5. Oxidative conversion of tris(4-methylbenzyl)amine to *p*-tolunitrile with I<sub>2</sub>

To a mixture of tris(4-methylbenzyl)amine (329.5 mg, 1 mmol) and aq NH<sub>3</sub> (3.0 mL, 45 mmol) was added I<sub>2</sub> (1.650 g, 6.5 mmol) at room temperature under an empty balloon. The resulting mixture was stirred at 60 °C. After 4 h at the same temperature, the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (3 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×15 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide *p*-tolunitrile in 84% 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.

#### 4.6. Typical procedure for oxidative conversion of primary alcohols to nitriles with DIH

To a mixture of 1-dodecanol (186.3 mg, 1 mmol) and aq NH<sub>3</sub> (3.0 mL, 45 mmol) was added DIH (731.9 mg, 2.0 mmol) at room temperature under an empty balloon. The obtained mixture was stirred at 60 °C. After 32 h at the same temperature, the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (3 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×15 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide laurionitrile in 97% yield in an almost pure state. If necessary, the product was purified by column chromatography on silica gel (hexane/EtOAc=4:1) to give pure laurionitrile as a colorless oil. IR (NaCl): 2250 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ=2.34 (2H, t, *J*=7.1 Hz), 1.66 (2H, quintet, *J*=7.1 Hz), 1.45 (2H, quintet, *J*=7.1 Hz), 1.29 (14H, br), 0.88 (3H, t, *J*=7.0 Hz).

#### 4.7. Typical procedure for oxidative conversion of primary amines to nitriles with DIH

To a mixture of 1-dodecylamine (185.4 mg, 1 mmol) and aq NH<sub>3</sub> (3.0 mL, 45 mmol) was added DIH (439.1 mg, 1.2 mmol) at room temperature under an empty balloon. The obtained mixture was stirred at 60 °C. After 6 h at the same temperature, the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (3 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×15 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide laurionitrile in 88% yield in an almost pure state. If necessary, the product was purified by column chromatography on silica gel (hexane/EtOAc=4:1) to give pure laurionitrile as a colorless oil.

#### 4.8. Typical procedure for oxidative conversion of aldehydes to nitriles with DIH

To a mixture of *p*-tolualdehyde (120.2 mg, 1 mmol) and aq NH<sub>3</sub> (3.0 mL, 45 mmol) was added DIH (219.6 mg, 0.6 mmol) at room temperature under an empty balloon. The obtained mixture was stirred at the same temperature

for 1 h. The reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (1 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×15 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide *p*-tolunitrile in 89% yield in an almost pure state. If necessary, the product was purified by column chromatography on silica gel (hexane/EtOAc=4:1) to give pure *p*-tolunitrile as a colorless solid.

#### 4.9. Typical procedure for oxidative conversion of imines to nitriles with I<sub>2</sub>

To a mixture of *N*-(4-methylbenzylidene)-1-dodecylamine (287.5 mg, 1 mmol) and aq NH<sub>3</sub> (3.0 mL, 45 mmol) was added I<sub>2</sub> (1.015 g, 4.0 mmol) at room temperature under an empty balloon. The obtained mixture was stirred at 60 °C. After 16 h at the same temperature, the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and satd aq Na<sub>2</sub>SO<sub>3</sub> (3 mL) at 0 °C, and was extracted with Et<sub>2</sub>O (3×15 mL). The organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> to provide *p*-tolunitrile and laurionitrile in 79% and 80%, respectively. The products were separated by column chromatography on silica gel (hexane/EtOAc=4:1) to give pure *p*-tolunitrile as a colorless solid and laurionitrile as a colorless oil.

**4.9.1. Benzonitrile.** IR (neat): 2230 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 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).

**4.9.2. 4-Chlorobenzonitrile.** IR (neat): 2225 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ=7.61 (2H, d, *J*=8.5 Hz), 7.47 (2H, d, *J*=8.5 Hz).

**4.9.3. 3-Nitrobenzonitrile.** IR (neat): 2237 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ=8.55 (1H, s), 8.49 (1H, d, *J*=8.1 Hz), 8.02 (1H, d, *J*=8.1 Hz), 7.75 (1H, t, *J*=8.1 Hz).

**4.9.4. 3-Cyanopyridine.** IR (neat): 2235 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ=8.91 (1H, s), 8.84 (1H, d, *J*=4.8 Hz), 7.99 (1H, d, *J*=8.0 Hz), 7.75 (1H, dd, *J*=8.0 and 4.8 Hz).

**4.9.5. 4-Methoxybenzonitrile.** IR (neat): 2224 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ=7.59 (2H, d, *J*=8.9 Hz), 6.96 (2H, d, *J*=8.9 Hz).

**4.9.6. 3,4,5-Trimethoxybenzonitrile.** IR (neat): 2225 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ=6.87 (2H, s), 3.90 (3H, s), 3.88 (6H, s).

**4.9.7. 2-Cyanothiophene.** IR (neat): 2224 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 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).

**4.9.8. 1-Naphthonitrile.** IR (neat): 2222 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 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).

**4.9.9. 2,5-Dimethylbenzonitrile.** IR (KBr): 2230 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ=7.39 (1H, s), 7.28 (1H, d, *J*=7.9 Hz), 7.19 (1H, d, *J*=7.9 Hz), 2.50 (3H, s), 2.34 (3H, s).

**4.9.10. 2,4,6-Trimethylbenzotrile.** IR (neat): 2220  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =6.93 (2H, s), 2.48 (6H, s), 2.32 (3H, s).

**4.9.11. Cinnamonitrile.** IR (neat): 2216  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =7.48–7.38 (5H, m), 7.41 (1H, d,  $J$ =16.7 Hz), 5.89 (1H, d,  $J$ =16.7 Hz).

**4.9.12. Terephthalonitrile.** IR (neat): 2229  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =7.80 (4H, s).

**4.9.13. 3-(4-Methoxyphenyl)propionitrile.** IR (neat): 2250  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =7.15 (2H, d,  $J$ =8.8 Hz), 6.87 (2H, d,  $J$ =8.8 Hz), 3.80 (3H, s), 2.90 (2H, t,  $J$ =7.4 Hz), 2.58 (2H, t,  $J$ =7.4 Hz).

**4.9.14. Tridecanenitrile.** IR (neat): 2247  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =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 (16H, br), 0.88 (3H, t,  $J$ =7.2 Hz).

**4.9.15. Cyclohexanecarbonitrile.** IR (neat): 2218  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =2.62 (1H, m), 1.85 (2H, m), 1.72 (4H, m), 1.55–1.37 (4H, m).

**4.9.16. 1-Cyanoadamantane.** IR (neat): 2229  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =2.04 (9H, br), 1.74 (6H, br).

**4.9.17. Sebaconitrile.** IR (neat): 2245  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =2.35 (4H, t,  $J$ =7.1 Hz), 1.66 (4H, quintet,  $J$ =7.1 Hz), 1.46 (4H, m), 1.35 (4H, m).

**4.9.18. 2-Chlorobenzonitrile.** IR (KBr): 2230  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =7.69 (1H, d,  $J$ =7.7 Hz), 7.58–7.51 (2H, m), 7.38 (1H, dd,  $J$ =7.7 and 6.7 Hz).

**4.9.19. 2-Methoxybenzotrile.** IR (neat): 2230  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =7.59–7.52 (2H, m), 7.01 (1H, t,  $J$ =7.5 Hz), 6.98 (1H, d,  $J$ =8.4 Hz).

**4.9.20. Isophthalonitrile.** IR (KBr): 2240  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =7.97 (1H, s), 7.92 (2H, d,  $J$ =8.1 Hz), 7.67 (1H, t,  $J$ =8.1 Hz).

**4.9.21. 4-Nitrobenzotrile.** IR (neat): 2233  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =8.37 (2H, d,  $J$ =8.9 Hz), 7.90 (2H, d,  $J$ =8.9 Hz).

**4.9.22. Suberonitrile.** IR (neat): 2250  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =2.37 (4H, t,  $J$ =7.0 Hz), 1.70 (4H, quintet,  $J$ =7.0 Hz), 1.52 (4H, m).

**4.9.23. 1-(*p*-Toluenesulfonyl)indole-3-carbonitrile.** Mp 155–157 °C. IR (neat): 2231  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =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).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm):  $\delta$ =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 (FAB): calcd for  $\text{C}_{16}\text{H}_{13}\text{O}_2\text{N}_2\text{S}$ : 297.0698; found:  $M+1=297.0687$ .

**4.9.24. 4-(*p*-Toluenesulfonyl)aminomethylbenzotrile.** Mp 110–112 °C (lit.<sup>13</sup> 112–114 °C). IR (neat): 2231  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$ =7.73 (2H, d,  $J$ =8.1 Hz), 7.54 (1H, d,  $J$ =7.8 Hz), 7.52 (1H, d,  $J$ =7.8 Hz), 7.42 (1H, s), 7.41 (1H, t,  $J$ =7.8 Hz), 7.32 (2H, d,  $J$ =8.1 Hz), 4.80 (1H, br s), 4.19 (1H, br d,  $J$ =6.5 Hz), 2.45 (3H, s).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm):  $\delta$ =143.9, 138.1, 136.6, 132.2, 131.3, 131.1, 129.8, 129.4, 127.0, 118.4, 112.5, 46.2, 21.5. HRMS (FAB): calcd for  $\text{C}_{15}\text{H}_{15}\text{O}_2\text{N}_2\text{S}$ : 287.0854; found:  $M+1=287.0853$ .

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