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Direct transformation of *N*,*N*-disubstituted amides and isopropyl esters to nitriles

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ABSTRACT

Various *N*,*N*-dimethyl amides, *N*-methoxy-*N*-methyl amides, and isopropyl esters were smoothly transformed into the corresponding nitriles in good to moderate yields by the treatment with diisobutylaluminium hydride, followed by treatment with molecular iodine in aq ammonia. The present reactions are novel one-pot and practical methods for the transformation of *N*,*N*-disubstituted amides and isopropyl esters into nitriles, through the formation of hemiaminal *O*-$AlBu_2$ and hemiacetal *O*-$AlBu_2$, respectively.

1. Introduction

Nitriles are one of the most important synthetic transformation precursors because they can be easily converted into amines, ketones, and nitrogen-containing heterocycles, such as tetrazoles and oxazoles, and are used as intermediates for the synthesis of agrochemicals, pharmaceuticals, and functional materials.[1] Citalopram hydrobromide® (treatment of alcohol dependency), Periciazine® (anti-psychotic drug), Fadrozole® (oncolytic drug), and Letrozole® (breast cancer therapy) are pharmaceutically important aromatic nitriles.[2] The most typical method for the preparation of nitriles is the dehydration of *N*-free amides with $SOCl_2$, TsCl/Py, P_2O_5, $POCl_3$, $COCl_2$, $TiCl_4$, $(CF_3CO)_2O$/Py, or Ph_3P/CCl_4.[3] Recently, aromatic nitriles have been prepared by the dehydration of aromatic amides with $(CH_2O)_n/HCO_2H$,[4a] $(COCl)_2$/DMSO,[4b] dibutyltin oxide/microwave,[4c] $Cp_2Zn(CH_3)_2$,[4d] $Cl_2P(O)OEt$/DBU,[4e] and $Ru_3(CO)_7/R_3SiH$.[4f] However, in those cases, *N*-free amides (primary amide) are required. Study of the transformation of *N*,*N*-dialkyl-substituted amides into the corresponding nitriles are extremely limited. One example is the transformation of *N*-benzyl or *N*-*tert*-butyl amides into the corresponding nitriles via *N*-benzyl or *N*-*tert*-butyl bond cleavage.[3] Thus, to the best of our knowledge, the practical one-pot transformation of *N*,*N*-dialkyl-substituted amides into the corresponding nitriles is not known. Moreover, few methods for the direct conversion of esters into nitriles are known. One example is the transformation of esters into the corresponding nitriles with dimethylaluminium amide via the formation of an amide intermediate in xylene refluxing conditions.[5a,b] A second example is the transformation of aromatic methyl esters into the corresponding aromatic nitriles with $NaN(SiMe_3)_2$ in a sealed tube at 185 °C.[5c] As far as we know, there are no practical, mild, and efficient methods for the transformation of esters into the corresponding nitriles. Molecular iodine (I_2) is one of the simplest oxidants currently available. It is highly affordable and has very low toxicity. Therefore, in view of environmentally benign organic synthesis, I_2 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.[6] As part of our ongoing studies on the use of I_2 for organic synthesis,[7] we would like to report herein the one-pot transformation of *N*,*N*-dimethyl amides and *N*-methoxy-*N*-methyl amides into the corresponding nitriles, and the one-pot transformation of isopropyl esters into the corresponding nitriles.

2. Results and discussion

Recently, we have reported a metal-free one-pot conversion of electron-rich aromatics into the corresponding aromatic nitriles in good yields. This method involved the formation of aromatic *N*,*N*-dimethyliminium salts with $POCl_3$ and DMF, followed by the treatment with I_2 in aq NH_3.[8a] We have also reported one-pot conversion of aromatic bromides and aromatics into the corresponding aromatic nitriles with *n*-BuLi and subsequently DMF, followed by the treatment with I_2 in aq NH_3.[8b,c] Based on those studies, we attempted to conduct a simple, practical, and one-pot transformation of *N*,*N*-disubstituted amides into the corresponding nitriles. The reaction was carried out as follows: diisobutylaluminium hydride (DIBAL-H) was added to a solution of *N*,*N*-dimethyl benzamide (**1A**-**a**) in THF at −78 °C. The reaction temperature was slowly increased from −78 °C to −40 °C. After 1.5 h, aq NH_3 (28.0–30.0%) and I_2 were added at 0 °C. After 2 h at room temperature, the reaction mixture was quenched with saturated aq Na_2SO_3 solution to give benzonitrile (**2A**) in 67% yield, as shown in Table 1. (entry 3, **1A**-**a**). When $LiAlH(O^tBu)_3$ was used instead of DIBAL-H, starting amide was recovered quantitatively even at 0 °C (entry 1, **1A**-**a**) and a mixture of benzonitrile and benzyl alcohol was obtained when $LiAlH_4$ was used (entry 2, **1A**-**a**). Among the three solvents, such

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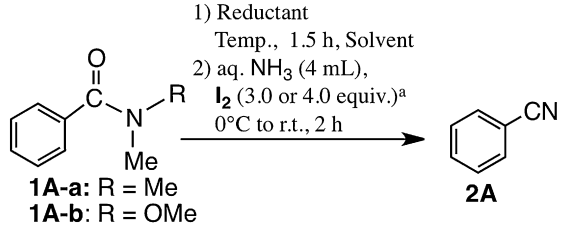
Table 1
Conversion of benzamide to benzonitrile

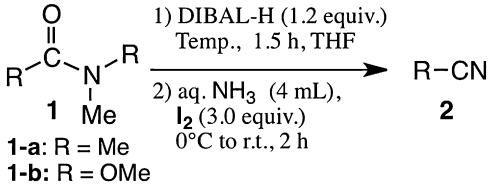


Entry	Reductant (equiv)	Temp °C	Solvent	**2A**/yields (%)	
				1A-a	**1A-b**
1	$LiAlH(O^tBu)_3$ (1.2)	0	THF	0 (98)[b]	—
2	$LiAlH_4$ (1.2)	0	THF	21 (32)[d]	—
3	DIBAL-H (1.2)	−78 to −40	THF	67 (3)[b]	68
4	DIBAL-H (1.2)	−78 to −40	CH_2Cl_2	55 (16)[b]	—
5	DIBAL-H (1.2)	−78 to −40	PhMe	52 (18)[b]	—
6	DIBAL-H (1.2)	0	THF	25 (16)[b]	62
7	DIBAL-H (1.2)	−78	THF	56	54
8	DIBAL-H (1.5)	−78 to−40	THF	55	—
9[c]	DIBAL-H (1.2)	−78 to −40	THF	59 (7)[b]	—

[a] **1A-a**/I_2 (3.0 equiv), **1A-b**/I_2 (4.0 equiv).
[b] Recovery yield of starting materials.
[c] Reaction temperature was 40 °C in the second step.
[d] Yield of benzyl alcohol.

as THF, CH_2Cl_2, and toluene, THF showed the best reactivity. The reaction temperature from −78 °C to −40 °C shown in entry 3 yielded the best results among the various reaction temperatures examined (entries 3–9, **1A-a**). The same treatment of *N*-methoxy-*N*-methyl benzamide (Weinreb amide, **1A-b**) with DIBAL-H, followed by treatment with I_2 in aq NH_3 provided benzonitrile (**2A**) in 68% yield under the same conditions (entry 3, **1A-b**). Based on these results, various aromatic amides (**1**), such as *N*,*N*-dimethyl *p*-chlorobenzamide, *N*,*N*-dimethyl *p*-bromobenzamide, *N*,*N*-dimethyl *p*-nitrobenzamide, *N*,*N*-dimethyl *p*-methylbenzamide, *N*,*N*-dimethyl *p*-methoxybenzamide, *N*,*N*-dimethyl 3-methylbenzamide, and *N*,*N*-dimethyl 3,4,5-trimethoxybenzamide could be transformed into the corresponding aromatic nitriles (**2**) in good to moderate yields under the same conditions with DIBAL-H, followed by treatment with I_2 in aq NH_3, as shown in Table 2 (entries 1–9, 11, 13, **1-a**). The same treatment of *N*,*N*-dimethyl 1-naphthalenecarboxyamide, *N*,*N*-dimethyl 2-naphthalenecarboxyamide, and heteroaromatic amides, such as *N*,*N*-dimethyl 3-

Table 2
Conversion of amides to nitriles



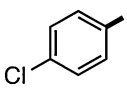
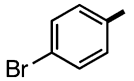
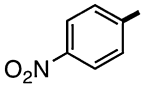
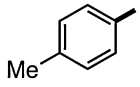
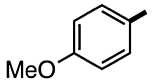
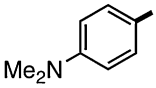
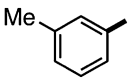
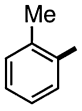
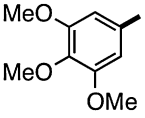
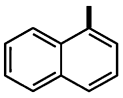
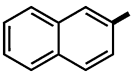
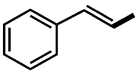
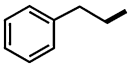
Entry	R−	Temp °C	**2**/Yields (%)	
			1-a	**1-b**
1		−78 to −40	67	68[b]
2		−78	76	78[c]
3		−78 to −40	85	—

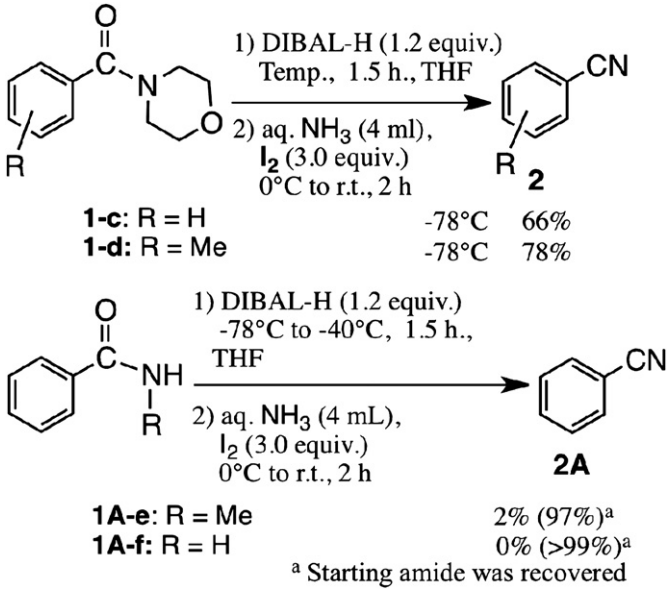
Table 2 (*continued*)

Entry	R−	Temp °C	**2**/Yields (%)	
			1-a	**1-b**
4		−78		82[c]
5		−78 to −40	87	—
6		−78 to −40	90	92[d]
7		−78	77	79[c]
8		−78 to −40	44	—
9		−78	73	75[d]
10		−78 to −40	33	71[c]
11		−78	58	74[c]
12		−78	20 (40)[a]	77[c]
13		−78	68	77[d]
14		−78	56 (29)[a]	98[d]
15		−78	90	88[c]
16		−78	39	83[c]
17		−78 to −40	64	59[d]
18		−78	13 (42)[a]	97[b]
19		−78 to −40	30	79[b]
20	$CH_3(CH_2)_{10}$—	−78 to −40	Trace	89[b]

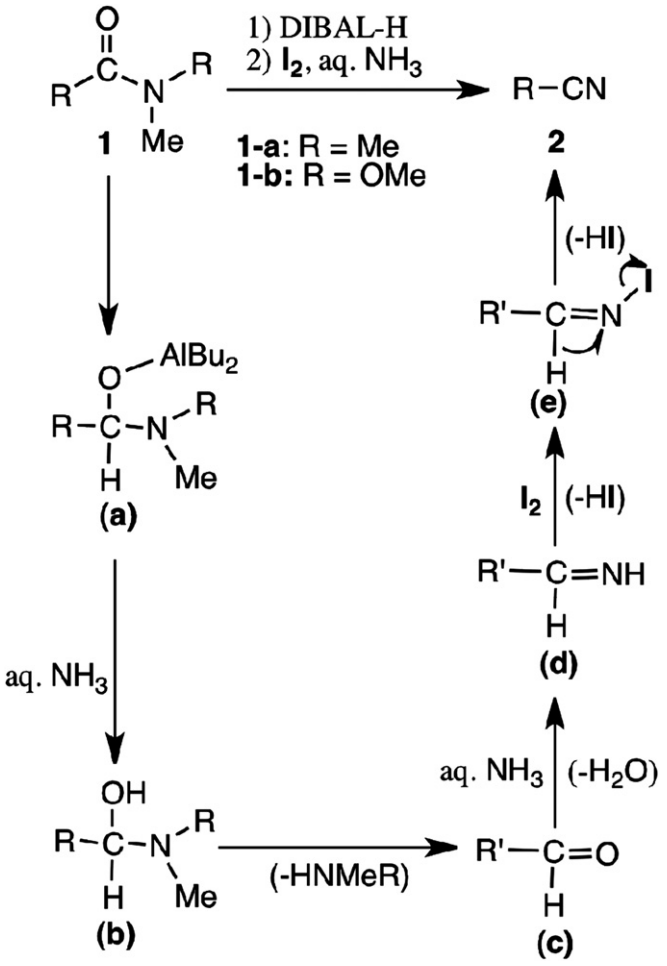
[a] Yield of recovered starting amide.
[b] I_2 (4.1 equiv) was used.
[c] I_2 (5.0 equiv) was used.
[d] I_2 (4.6 equiv) was used.

pyridinecarboxyamide with DIBAL-H, followed by the treatment with aq NH_3 and I_2, provided the corresponding aromatic nitriles in good to moderate yields (Table 2, entries 14, 15, 17, **1**-**a**). On the other hand, when *N*,*N*-dimethyl *p*-(dimethylamino)benzamide, *N*,*N*-dimethyl 2-methylbenzamide and *N*,*N*-dimethyl 2-thiophenecarboxyamide were used, the yields of nitriles were low and the recovery of starting amide and the formation of alcohol were observed (Table 2, entries 10, 12, 16, **1**-**a**). However, when *N*-methoxy-*N*-methyl *p*-(dimethylamino)benzamide, *N*-methoxy-*N*-methyl 2-methylbenzamide, and *N*-methoxy-*N*-methyl 2-thiophenecarboxyamide were used under the same conditions, *p*-(*N*,*N*-dimethylamino)benzonitrile, 2-methylbenzonitrile, and 2-cyanothiophene could be obtained in good yields (Table 2, entries 10, 12, 16, **1**-**b**). Then, the same transformation of *N*,*N*-disubstituted α,β-unsaturated amide and aliphatic amides into the corresponding nitriles was studied. When *N*,*N*-dimethyl cinnamamide, *N*,*N*-dimethyl dihydrocinnamamide, and *N*,*N*-dimethyl dodecanamide were treated with DIBAL-H, followed by the treatment with aq NH_3 and I_2 under the same conditions, the yields of the corresponding nitriles were low to poor (Table 2, entries 18–20, **1**-**a**). However, when *N*-methoxy-*N*-methyl cinnamamide, *N*-methoxy-*N*-methyl dihydrocinnamamide, and *N*-methoxy-*N*-methyl dodecanamide were treated with DIBAL-H, followed by the treatment with aq NH_3 and I_2 under the same conditions, the corresponding amides (**2**) were obtained in very good yields (Table 2, entries 18–20, **1**-**b**). Together, the results show that the reactivity of *N*-methoxy-*N*-methyl amides **1**-**b** is higher than that of *N*,*N*-dimethyl amides **1**-**a**, probably due to the high electrophilicity of the carbonyl group of *N*-methoxy-*N*-methyl amides. Then, morpholine benzamide (**1**-**c**) and morpholine *p*-methylbenzamide (**1**-**d**), instead of *N*,*N*-dimethyl benzamide (**1A**-**a**) or *N*-methoxy-*N*-methyl benzamide (**1A**-**b**) were treated with DIBAL-H under the same conditions to generate benzonitrile and *p*-methylbenzonitrile, respectively, in good yields, as shown in Scheme 1. While, the starting amides were recovered quantitatively when *N*-methyl benzamide (**1A**-**e**) (secondary amide) and benzamide (**1A**-**f**) (primary amide) were used. Thus, the present reaction is an effective method for the direct transformation of *N*,*N*-disubstituted amides into the corresponding nitriles.

A plausible reaction mechanism is shown in Scheme 2. The initial step is the formation of hemiaminal *O*-$AlBu_2$ (**a**) by the reduction of *N*,*N*-disubstituted amide (**1**) with DIBAL-H. Then, hemiaminal *O*-$AlBu_2$ (**a**) reacts with aq NH_3 to form imine (**d**) through the formation of hemiaminal (**b**) and aldehyde (**c**). Imine (**d**) further reacts with I_2 in aq NH_3 to form *N*-iodo imine (**e**). Once *N*-iodo imine (**e**) is formed, HI elimination smoothly occurs by the reaction with NH_3 to generate aromatic nitrile (**2**).



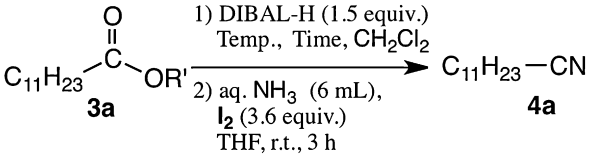
Scheme 1.



Scheme 2. Plausible reaction mechanism.

Then, the direct transformation of esters into the corresponding nitriles was studied. The reaction was carried out as follows: DIBAL-H was added to a solution of isopropyl dodecanoate (**3a**) in dichloromethane at −78 °C. The reaction mixture was stirred for 3 h at the same temperature. Then, aq NH_3 (28.0–30.0%) and I_2 were added, and the reaction mixture was warmed to room temperature. After 3 h, the reaction mixture was quenched with saturated aq Na_2SO_3 solution to give dodecanenitrile (**4a**) in 78% yield, as shown in Table 3 (entry 7). Among methyl, 2,2,2-trifluoroethyl, propyl, and isopropyl dodecanoates, isopropyl dodecanoate gave the best result. The reaction of 2,2,2-trifluoroethyl ester did not generate dodecanenitrile (**4a**), while a mixture of starting material and 1-dodecanol was obtained (entries 3, 4). When methyl ester and *n*-propyl esters were used, a mixture of dodecanenitrile (**4a**) and 1-dodecanol was obtained (entries 1, 2, 5, 6). Based on these results, various isopropyl esters (**3**), such as isopropyl octanoate, isopropyl decanoate, isopropyl tetradecanoate, isopropyl 3-phenylpropanoate, isopropyl 4-phenylbutanoate, isopropyl 5-phenylpentanoate, and isopropyl 3-(4′-fluorophenyl)propanoate, were treated with DIBAL-H, followed by the treatment with I_2 and aq NH_3 to provide the corresponding nitriles (**4**) in good yields, as shown in Table 4 (entries 1–8). The same treatment of isopropyl 1-adamantanecarboxylate, which has a tertiary alkyl group, gave

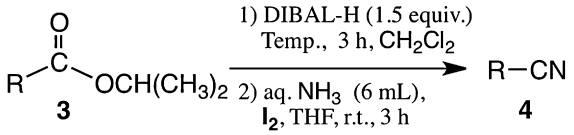
Table 3
Conversion of undecanoate esters to dodecanenitrile

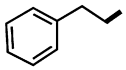
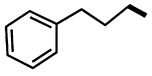
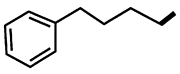
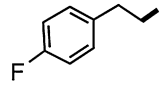
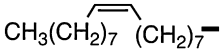
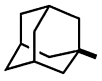


Entry	R′—	Temp °C	Time h	Yields (%)
1	CH_3	−78	3	52 (26)[a]
2	CH_3	−78 to −60	2	41 (58)[a]
3	CH_2CF_3	−78	3	0 (58)[a] (21)[b]
4	CH_2CF_3	−78 to −60	2	0 (58)[a] (23)[b]
5	$CH_2CH_2CH_3$	−78	3	72 (14)[a]
6	$CH_2CH_2CH_3$	−78 to −60	2	54 (40)[a]
7	$CH(CH_3)_2$	−78	3	78 (6)[a]
8	$CH(CH_3)_2$	−78 to −60	2	77 (6)[a]

[a] Yield of alcohol.
[b] Yield of starting ester.

Table 4
Conversion of isopropyl esters to nitriles

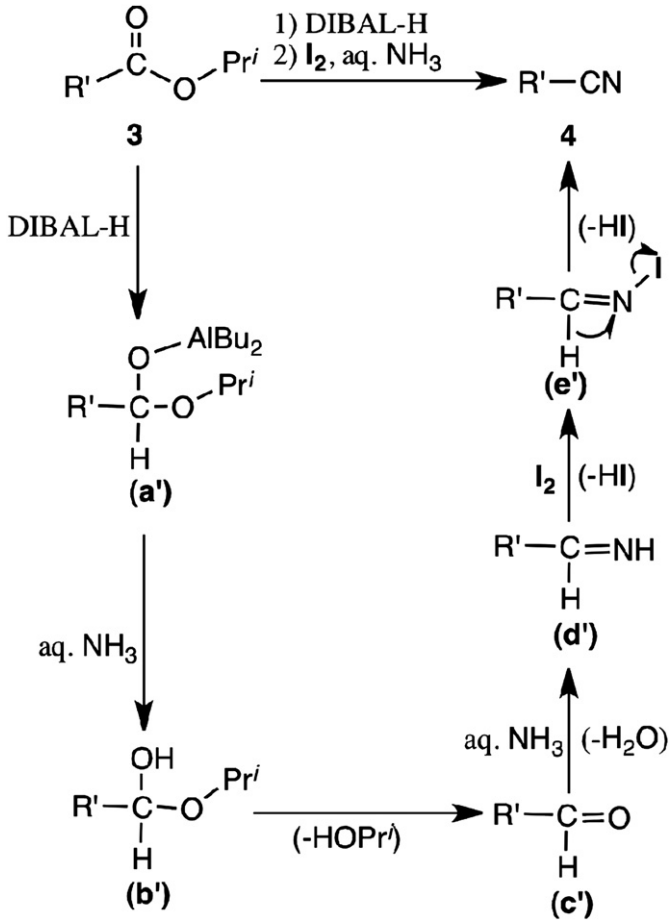


Entry	R—	Temp	I_2 (equiv)	Yield (%)
1	$CH_3(CH_2)_6$—	−78 to −60[a]	4.1	82
2	$CH_3(CH_2)_8$—	−78	4.1	82
3	$CH_3(CH_2)_{10}$—	−78	3.6	78
4	$CH_3(CH_2)_{12}$—	−78	3.6	90
5		−78	3.6	94
6		−78	3.6	68
7		−78	3.1	86
8		−78	3.1	86
9		−78	3.1	76
10		−78 to −60[a]	3.1	72

[a] Reaction time at the first step was 2 h.

1-adamantanecarbonitrile in good yield (entry 10). Moreover, the same treatment of isopropyl oleate, which has an olefinic group, generated the corresponding unsaturated nitrile in good yield (entry 9). Thus, the present reaction can be used for isopropyl esters bearing an olefinic group.

A plausible reaction mechanism is shown in Scheme 3. The initial step is the formation of hemiacetal *O*-$AlBu_2$ (**a′**) by the reduction of isopropyl ester (**3**) with DIBAL-H. Then, hemiacetal *O*-$AlBu_2$ (**a′**) generates aldehyde (**c′**), which reacts with aq NH_3 to form imine (**d′**). Imine (**d′**) further reacts with I_2 in aq NH_3 to form *N*-iodo imine (**e′**). Once *N*-iodo imine (**e′**) is formed, HI elimination



Scheme 3. Plausible reaction mechanism.

smoothly occurs by the reaction with NH_3 to generate aliphatic nitrile (**4**).

3. Conclusion

Various *N*,*N*-dimethyl amides and *N*-methoxy-*N*-methyl amides were transformed efficiently into the corresponding nitriles in good to moderate yields with DIBAL-H, followed by the treatment with I_2 in aq NH_3. Moreover, various aliphatic isopropyl esters were transformed into the corresponding aliphatic nitriles in good yields with DIBAL-H, followed by the treatment with I_2 in aq NH_3. Both reactions are novel and practical one-pot methods for the transformation of *N*,*N*-disubstituted amides and isopropyl esters into the corresponding nitriles.

4. Experimental

4.1. General

^1H NMR and ^{13}C NMR spectra were obtained with JEOL-JNM-ECX400, JEOL-JNM-ECS400, and JEOL-JNM-ECA500 spectrometers. Chemical shifts are expressed in parts per million downfield from TMS in δ units. Mass spectra were recorded on JMS-T100GCV, JMS-HX110, and Thermo LTQ Orbitrap 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 experimental procedure for the conversion of *N,N*-dialkyl amides (1) into nitriles (2)

To a solution of *N,N*-dimethyl benzamide (298 mg, 2 mmol) in dry THF (4 mL) was added DIBAL-H (1.04 M in hexane, 2.3 mL, 1.2 equiv) at −78 °C. The mixture was stirred for 1.5 h under an argon atmosphere at from −70 °C to −40 °C slowly. Then, aq NH_3 (concentration: 28.0–30.0%, 4 mL) and I_2 (762 mg, 3.0 equiv) were added at 0 °C, and the reaction mixture was stirred for 2 h at room temperature. Reaction mixture was poured into saturated aq Na_2SO_3 solution (10 mL) and extracted with ethyl acetate (15 mL×3). The organic layer was dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by short column chromatography on silica gel (eluent: hexane/ethyl acetate=4:1) to afford benzonitrile in 67% yield (138 mg).

Most of the present prepared nitriles are commercially available and they are identified with authentic nitrile compounds.

4.2.1. Benzonitrile. Colorless oil (commercial); IR (neat): 2230 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.67 (d, 2H, J=7.70 Hz), 7.61 (t, 1H, J=7.70 Hz), 7.48 (t, 2H, J=7.70 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ=132.7, 132.1, 129.1, 118.8, 112.4.

4.2.2. p-Chlorobenzonitrile. Mp 92–94 °C (commercial, mp 92 °C); IR (Nujol): 2225 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.61 (d, 2H, J=8.61 Hz), 7.47 (d, 2H, J=8.61 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ=139.5, 133.4, 129.7, 117.9, 110.8.

4.2.3. p-Bromobenzonitrile. Mp 114–115 °C (commercial, mp 113 °C); IR (Nujol): 2223 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.64 (d, 2H, J=8.59 Hz), 7.53 (d, 2H, J=8.59 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ=133.4, 132.6, 128.0, 118.0, 111.2.

4.2.4. p-Nitrobenzonitrile. Mp 145–147 °C (commercial, mp 147 °C); IR (Nujol): 2232 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=8.37 (d, 2H, J=8.90 Hz), 7.90 (d, 2H, J=8.90 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ=150.0, 133.5, 124.3, 118.2, 116.8.

4.2.5. 4-Methylbenzonitrile. Colorless oil (commercial); IR (neat): 2228 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.53 (d, 2H, J=8.60 Hz), 7.27 (d, 2H, J=8.60 Hz), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=143.6, 132.0, 129.8, 119.1, 109.2, 21.7.

4.2.6. 4-Methoxybenzonitrile. Mp 60–62 °C (commercial, 60 °C); IR (Nujol): 2217 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.59 (d, 2H, J=8.38 Hz), 6.95 (d, 2H, J=8.38 Hz), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=162.8, 133.9, 119.2, 114.7, 103.9, 55.1.

4.2.7. p-(N,N-Dimethylamino)benzonitrile. Mp 75–77 °C (commercial, mp 75 °C); IR (neat): 2210 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.46 (d, 2H, J=7.00 Hz), 6.64 (d, 2H, J=7.00 Hz), 3.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=152.4, 133.3, 120.7, 111.4, 97.4, 39.9.

4.2.8. 3-Methylbenzonitrile. Colorless oil (commercial); IR (neat): 2229 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.43–7.47 (m, 2H), 7.40 (d, 1H, J=8.05 Hz), 7.33–7.37 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=139.1, 133.5, 132.3, 129.1, 128.9, 118.9, 112.1, 21.0.

4.2.9. 2-Methylbenzonitrile. Colorless oil (commercial); IR (neat): 2225 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.59 (d, 1H, J=7.73 Hz), 7.48 (t, 1H, J=7.73 Hz), 7.32 (d, 1H, J=7.73 Hz), 7.27 (t, 1H, J=7.73 Hz); ^{13}C NMR (125 MHz, $CDCl_3$), 132.6, 132.5, 130.2, 126.2, 118.1, 112.7, 20.4.

4.2.10. 3,4,5-Trimethoxybenzonitirle. Mp 92–93 °C (lit.[9] mp 92–94 °C); IR (Nujol): 2224 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=6.87 (s, 2H), 3.90 (s, 3H), 3.88 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=153.5, 142.3, 118.9, 109.4, 106.7, 61.0, 56.3.

4.2.11. 1-Naphthonitrile. Mp 35–36 °C (commercial, mp 36–38 °C); IR (neat): 2222 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=8.22 (d, 1H, J=8.38 Hz), 8.06 (d, 1H, J=8.38 Hz), 7.93–7.88 (m, 2H), 7.68 (t, 1H, J=8.38 Hz), 7.61 (t, 1H, J=8.38 Hz), 7.51 (dd, 1H, J=7.25 Hz, 8.38 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ=133.2, 132.8, 132.6, 132.3, 128.6, 128.5, 127.5, 125.1, 124.8, 117.8, 110.1.

4.2.12. 2-Naphthonitrile. Mp 68–70 °C (commercial, mp 66–67 °C); IR (Nujol): 2225 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=8.24 (s, 1H), 7.95–7.87 (m, 3H), 7.68–7.58 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=133.2, 132.8, 132.6, 132.3, 128.6, 128.5, 127.5, 125.1, 124.8, 117.8, 110.1.

4.2.13. 2-Cyanothiophene. Colorless oil (commercial); IR (neat): 2222 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.64 (dd, 1H, J=3.85, 1.13 Hz), 7.62 (dd, 1H, J=4.98, 1.13 Hz), 7.14 (dd, 1H, J=4.98 Hz, 3.85 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ=137.3, 132.5, 127.6, 114.1, 109.8.

4.2.14. 3-Cyanopyridine. mp 49–51 °C (commercial, mp 50 °C); IR (Nujol): 2229 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=8.91 (sd, 1H, J=2.00 Hz), 8.83 (dd, 1H, J=4.87, 2.00 Hz), 7.99 (dt, 1H, J=7.95, 2.00 Hz), 7.46 (ddd, 1H, J=7.95, 4.87, 0.86 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ=153.0, 152.5, 139.2, 123.6, 116.5, 110.1.

4.2.15. Cinnamnitrile. Colorless oil (commercial); IR (neat): 2217 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.39–7.47 (m, 6H), 5.88 (d, 1H, J=16.90 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ=150.6, 133.6, 131.2, 129.1, 127.3, 118.1, 96.3.

4.2.16. 3-Phenylpropanenitrile. Colorless oil (commercial); IR (neat): 2247 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=7.33 (t, 2H, J=8.30 Hz), 7.26 (t, 1H, J=8.30 Hz), 7.22 (d, 2H, J=8.30 Hz), 2.93 (t, 2H, J=7.45 Hz), 2.59 (t, 2H, J=7.45 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ=138.0, 128.7, 128.2, 127.1, 119.0, 31.4, 19.2.

4.3. Typical procedure for the conversion of isopropyl esters (3) into nitriles (4)

To a solution of isopropyl tetradecanoate (555 mg, 2.05 mmol) in CH_2Cl_2 (2 mL) was added DIBAL-H (1.04 M in hexane, 3 mL, 1.5 equiv) at −78 °C. The mixture was stirred for 3 h at −78 °C under argon atmosphere. Then, aq NH_3 (6 mL), THF (3 mL), and I_2 (1.85 mg, 7.30 mmol) were added. The resulting solution was warmed to room temperature and stirred for 3 h. Reaction mixture was poured into saturated aq Na_2SO_3 solution (10 mL) and extracted with chloroform (15 mL×3). The organic layer was dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by short column chromatography on silica gel to give tetradecanenitrile in 90% (386 mg).

4.3.1. Octanenitrile. Colorless oil (commercial); IR=2247 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=0.89 (t, J=6.8 Hz, 3H), 1.27–1.38 (m, 6H), 1.41–1.48 (m, 2H), 1.62–1.70 (m, 2H), 2.34 (t, J=7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=14.0, 17.1, 22.5, 25.3, 28.4, 28.6, 31.5, 119.9.

4.3.2. Decanenitrile. Colorless oil (commercial); IR=2247 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=0.88 (t, J=6.9 Hz, 3H), 1.22–1.29 (m, 10H), 1.41–1.48 (m, 2H), 1.62–1.69 (m, 2H), 2.34 (t, J=7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=14.1, 17.1, 22.6, 25.3, 28.6, 28.7, 29.1, 29.2, 31.8, 119.9.

4.3.3. Dodecanenitrile. Colorless oil (commercial); IR=2246 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=0.88 (t, J=6.9 Hz, 3H), 1.21–1.30 (m,

14H), 1.41–1.46 (m, 2H), 1.62–1.69 (m, 2H), 2.33 (t, J=7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=14.1, 17.1, 22.7, 25.4, 28.6, 28.7, 29.3, 29.48, 29.53, 31.9, 119.9.

4.3.4. Tetradecanenitrile. Colorless oil (commercial); IR=2247 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=0.88 (t, J=6.7 Hz, 3H), 1.24–1.34 (m, 18H), 1.41–1.48 (m, 2H), 1.62–1.69 (m, 2H), 2.33 (t, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=14.1, 17.1, 22.7, 25.3, 28.6, 28.7, 29.27, 29.31, 29.5, 29.56, 29.60, 31.9, 119.8.

4.3.5. 4-Phenylbutanenitrile. Colorless oil (commercial); IR=2246 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.98 (m, 2H), 2.32 (t, J=7.2 Hz, 2H), 2.78 (t, J=7.2 Hz, 2H), 7.17–7.25 (m, 3H), 7.31 (t, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=16.3, 26.9, 34.3, 119.5, 126.5, 128.3, 128.4, 128.6, 139.7.

4.3.6. 5-Phenylpentanenitrile. Colorless oil; IR=2246 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.64–1.71 (m, 2H), 1.75–1.82 (m, 2H), 2.33 (t, J=7.2 Hz, 2H), 2.65 (t, J=7.2 Hz, 2H), 7.15–7.21 (m, 3H), 7.29 (t, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=17.0, 24.8, 30.2, 34.9, 119.6, 126.0, 128.3, 128.4, 141.2; HRMS (APPI) calcd for $C_{11}H_{13}N$ M=159.1043, obsd M^+=159.1037.

4.3.7. 3-(4′-Fluorophenyl)propanenitrile. Colorless oil; IR=2247 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=2.60 (t, J=7.3 Hz, 2H), 2.93 (t, J=7.3 Hz, 2H), 7.03 (t, J_{H-H} and J_{H-F}=8.8 Hz, 2H), 7.11 (dd, J_{H-H}=8.8 Hz, J_{H-F}=5.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=19.5, 30.7, 115.6, 115.8, 129.9 (d, J_{C-F}=8.4 Hz), 133.7, 162.0 (d, J_{C-F}=244.7 Hz); HRMS (APCI) calcd for C_9H_9NF M=150.0714, obsd M^+=159.0713.

4.3.8. 9-Octadecenenitrile. Colorless oil (commercial); IR=1654, 2247 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=0.88 (t, J=6.9 Hz, 3H), 1.26–1.37 (m, 20H), 1.63–1.69 (m, 2H), 1.99–2.03 (m, 4H), 2.33 (t, J=7.2 Hz, 2H), 5.31–5.39 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=14.1, 17.1, 22.7, 25.3, 27.1, 27.2, 28.6, 28.7, 28.9, 29.3, 29.5, 29.6, 29.7, 31.9, 119.8, 129.5, 130.1; HRMS (APPI) calcd for $C_{18}H_{33}N$ M 263.2608, obsd M^+=263.2604.

4.3.9. 1-Adamantanecarbonitrile. Mp 192–195 °C (commercial, mp 195 °C); IR=2229 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.70–1.78 (m, 6H), 2.04–2.08 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=27.0, 30.1, 35.7, 39.8, 125.3.

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Supplementary data

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