Transformation of aromatic bromides into aromatic nitriles with *n*-BuLi, pivalonitrile, and iodine under metal cyanide-free conditions

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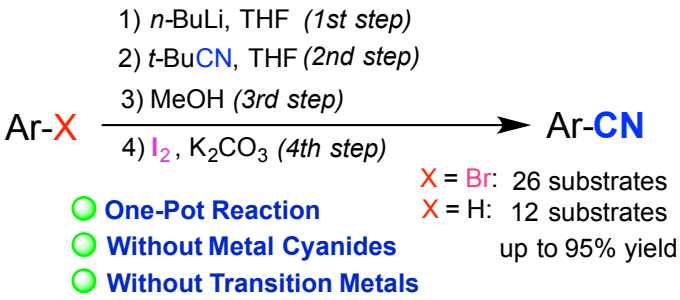
1) n-BuLi, THF (1st step)
2) t-BuCN, THF (2nd step)
3) MeOH (3rd step)
Ar-X
4) I2 , K2CO3 (4th step)
Ar-CN
X = Br: 26 substrates
X = H: 12 substrates
up to 95% yield
One-Pot Reaction
Without Metal Cyanides
Without Transition Metals

Graphical Abstract

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Transformation of Aromatic Bromides into Aromatic Nitriles with *n*-BuLi, Pivalonitrile, and Iodine under Metal Cyanide-Free Conditions

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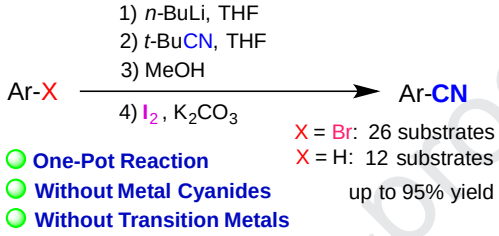

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Transformation of Aromatic Bromides into Aromatic Nitriles with *n*-BuLi, Pivalonitrile, and Iodine under Metal Cyanide-Free Conditions

Ko Uchida and Hideo Togo*[*]

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Abstract—Various aromatic nitriles could be obtained in good yields by the treatment of aryl bromides with *n*-butyllithium and then pivalonitrile, followed by the treatment with molecular iodine at 70 °C, without metal cyanides under transition-metal-free conditions. The present reaction proceeds through the radical β-elimination of imino-nitrogen-centered radicals formed from the reactions of imines and *N*-iodoimines under warming conditions.

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1. Introduction

Aromatic nitriles are one of the most important compounds, because there are components of well-known pharmaceuticals, such as Febuxostat (anti-podagric drug), Letrozole (breast cancer drug), and Fadrozole (breast cancer drug), *etc*., as well as liquid crystal materials, such as 4-cyano-4'-pentylbiphenyl, as shown in Fig. 1.[1] Aromatic nitriles can be smoothly transformed into aromatic amides, aromatic carboxylic acids, aromatic esters, benzylic amines, and nitrogen-containing heteroaromatics, such as 5-aryltetrazoles, 2-aryloxazoles, and 2-arylthiazoles.[1] Extensive synthetic studies of aromatic nitriles have been carried out.[2] Conventionally, aromatic nitriles have been prepared by the dehydration of primary aromatic amides with P_2O_5, $POCl_3$, or Ph_3P/CCl_4[3a,3b] and the Sandmeyer reaction of aromatic diazonium salts with CuCN.[3c]

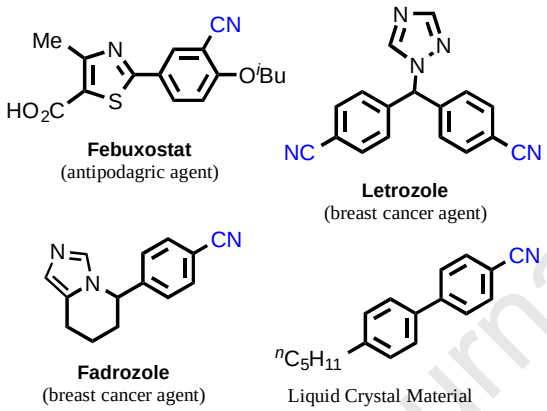


Fig.1 Pharmaceuticals and Liquid Crystal Material bearing Aromatic Nitrile Group

Recent typical studies for the preparation of aromatic nitriles are as follows:[4] the dehydration of primary aromatic amides with $(COCl)_2$, Et_3N, and Ph_3PO;[4a] the dehydrogenative cyanation of aldehydes via oximes with NH_2OH, SO_2F_2, and Et_3N;[4b] the Cu-catalyzed cyanation of aryl halides with α-iminonitrile, $Pd(OAc)_2$, and $Cu(TFA)_2$;[4c] the Pd-catalyzed cyanation of aryl bromides with XantPhos-$PdCl_2$ and $Zn(CN)_2$;[4d] the Pd-catalyzed cyanation of aryl chlorides with $Pd(OAc)_2$, tetraadamantylbiphosphine (TABP), and $K_4[Fe(CN)_6]$;[4e] the Ni-catalyzed cyanation of phenol derivatives with $Zn(CN)_2$;[4f] the acridinium-catalyzed cyanation of arenes with TMSCN and acridinium salt under LED irradiation;[4g] the Rh-catalyzed cyanation of 2-aryl-1,2,3-triazoles with *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide and $[Cp^*RhCl_2]_2$;[4h] the α-cyanation of pyridines with *O*-methanesulfonyl α-chloroaldoximes;[4i] the Rh-catalyzed cyanation of 2-arylpyridines with *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide and AgOAc;[4j] the Co-catalyzed cyanation of 2-arylpyridines with *N*-cyano-*N*-aryl-*p*-toluenesulfonamides and $AgSbF_6$;[4k] the Pd-catalyzed cyanation of arenes with AgCN;[4l] the Rh-catalyzed cyanation of 2-arylpyridines with 2,2-dicyanopropane and CuO;[4m] and the electrochemical cyanation of electron-rich arenes with NaCN using Pt electrodes.[4n]

However, most of those methods require metal cyanides and/or transition metals, such as Pd, Cu, *etc*. We have reported the preparation of aromatic nitriles from benzylic alcohols and amines,[5a] from benzylic halides,[5b] from aromatic esters,[5c,5d] from arenecarboxylic acids,[5e] from aryl bromides,[5f,5g] from arenes,[5h~5j] from phenols,[5k] and from methylarenes[5l,5m] using molecular iodine and aq. ammonia, without using any metal cyanides and transition metals.

On the other hand, recently, synthetic studies of imino-nitrogen-centered radicals and imino-carbon-centered radicals have become popular, especially for the preparation of nitrogen-containing heterocycles, such as phenanthridines.[6] Most of the precursors of imino-nitrogen-centered radicals are oxime derivatives, such as *O*-aroyl esters of oximes, *O*-aryl oximes, *etc*., and recently, the conversion of *O*-phenyl oximes into 1,2-aminoalcohols with $Ir(ppy)_2(dtbbpy)PF_6$ under blue LED irradiation[6g] and the conversion of imidates into 1,2-aminoalcohols with NaI and $PhI(OAc)_2$,[6h] and with NIS and Ag_2O[6i] via oxazolines were reported. The synthetic use of imino-nitrogen-centered radicals derived from aromatic nitriles is also known. For example, treatment of *N*-aryl acrylamides bearing a cyano group on the aromatic ring with $BrCH_2CN$ in the presence of *fac*-$Ir(ppy)_3$ under blue LED irradiation[7a] and with CF_3SO_2Cl in the presence of $Ru(phen)_3Cl_2$ under blue LED irradiation[7b] via radical *6-exo-dig* cyclization of the formed carbon-centered radicals to the nitrile group, followed by cyclization of the formed imino-nitrogen-centered radical onto the aromatic ring was reported.

In addition, recent studies of radical β-cleavage reactions of imino-nitrogen-centered radicals formed from *O*-aroyl or *O*-aryl cyclobutanone oximes and cyclopentanone oximes to generate butyronitrile and valeronitrile derivatives, respectively, have become popular, as follows:[8] the β-cleavage reactions of *O*-aroyl cyclobutanone oximes with styrenes in the presence of $Cu(CH_3CN)_4PF_6$ under blue LED irradiation;[8a] *O*-aroyl cyclobutanone oximes with diaryl disulfides in the presence of *fac*-$Ir(ppy)_3$ under blue LED irradiation;[8b] *O*-aroyl cyclobutanone oximes with *O*-vinyl triflates in the presence of $Cu(OAc)_2$ at 100 °C;[8c] *O*-aroyl cyclobutanone oximes with arenethiols in the presence of $Cu(OTf)_2$ at r.t.;[8d] and *O*-phenyl cyclobutanone oximes and cyclopentanone oximes with TEMPO under microwave irradiation.[8e] Moreover, the formation of aromatic nitriles from *O*-acetyl alkyl aryl ketone oximes in the presence of CuI in DMSO at 90 °C through the generation of the corresponding imino-nitrogen-centered radicals was recently reported.[8f]

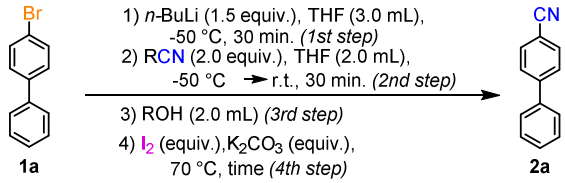
Previously, we reported the one-pot preparation of 6-aryl- and 6-alkylphenanthridines from *o*-cyanobiaryls by the reaction with aryllithiums or alkyllithiums, followed by the

reaction with water and then molecular iodine at 60 °C for 2 h through the formation of *N*-iodoimines and imino-nitrogen-centered radicals.[9] Additionally, reaction of aryl Grignard reagents (ArMgBr) with pivalonitrile at 60 °C, followed by the reaction with $CuBr_2$ (0.1 equiv.) under oxygen atmosphere at 80 °C was reported to form aromatic nitriles.[10] Based on those studies, here, we would like to report the transformation of aryl bromides and arenes into the corresponding aromatic nitriles by the treatment with *n*-BuLi and then pivalonitrile, followed by the reaction with molecular iodine through the radical β-elimination of imino-nitrogen-centered radicals under metal-cyanide-free and transition-metal-free conditions.

2. Results and Discussion

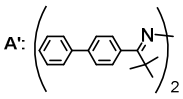
First, 4-bromobiphenyl **1a** (3.0 mmol) in THF (3 mL) was treated with *n*-BuLi (1.5 equiv.) at -50 °C for 0.5 h to form 4-biphenyl anion (1st step). Treatment of the formed 4-biphenyl anion with pivalonitrile (2.0 equiv.) in the temperature range of -50 °C to room temperature for 0.5 h (2nd step), followed by the reaction with water (4.0 mL, 3rd step), and then with molecular iodine (1.5 equiv.) and K_2CO_3 (3.0 equiv.) at 70 °C for 1 h (4th step) gave 4-cyanobiphenyl **2a** in 35% yield, together with *p*-biphenyl *t*-butyl ketone, a hydrolyzed product of the formed imine, in 45% yield, as shown in Table 1 (entry 1). To suppress the formation of the ketone, the formed 4-biphenyl anion was treated with MeOH (2.0 mL, 3rd step) and then with molecular iodine (3.0 equiv.) and K_2CO_3 (3.0 equiv.) at 70 °C for 5 h (4th step) to give 4-cyanobiphenyl **2a** in 74% yield, together with *p*-biphenyl *t*-butyl ketone in 13% yield (entry 2). Moreover, treatment of 4-biphenyl anion with MeOH (2.0 mL, 3rd step) and then with molecular iodine (4.0 equiv.) and K_2CO_3 (4.0 equiv.) at 70 °C for 6 h (4th step) gave 4-cyanobiphenyl **2a** in 84% yield, without the ketone (entry 4). However, when the 4th reaction step in entry 4 was carried out at 30 °C for 24 h, the yield of 4-cyanobiphenyl **2a** was 40% (entry 3). As a gram-scale experiment, treatment of 4-bromobiphenyl **1a** (6.0 mmol) under the same procedure and conditions as those in entry 4 gave 4-cyanobiphenyl **2a** in 94% yield (entry 4). When the reaction mixture after the 3rd reaction step in entry 4 was irradiated with a tungsten lamp (300 W) for 6 h in the temperature range of 35 °C~40 °C (4th step), instead of the warming treatment at 70 °C, 4-cyanobiphenyl **2a** was again obtained in 81% yield (entry 5). When *t*-BuOH and CF_3CH_2OH instead of MeOH were used in the 3rd reaction step under the same procedure and conditions as those in entry 4, the yields of 4-cyanobiphenyl **2a** were decreased to 70% and 54%, and the ketone was obtained in 20% and 33% yields, respectively (entries 6, 7). Moreover, when the reaction mixture in the 3rd reaction step was directly treated with molecular iodine at 70 ° C for 115 h without quenching by MeOH, the yield of 4-cyanobiphenyl **2a** was dramatically decreased to 5%, and the ketone and imine-coupling product **A'** were obtained in 68% and 10% yields, respectively (entry 8). Probably, direct addition of molecular iodine to the formed imino-anion induces rapid formation of *N*-iodoimine, and smooth formation of imino-nitrogen-centered radical occurs to form imine-coupling product **A'**. In the present reaction, Na_2CO_3 instead of K_2CO_3 could be also used at 4th reaction step under the same procedure and conditions as those of entry 4 to give 4-cyanobiphenyl **2a** in 78% yield. However, when K_2CO_3 was not added at 4th reaction step, yield of 4-cyanobiphenyl **2a** was decreased to 59% yield, together with *p*-biphenyl *t*-butyl ketone in 30% yield. Thus, the addition of base, such as K_2CO_3, is important to get aromatic nitrile in good yield. When the same reaction with 4-bromobiphenyl **1a** was carried out with isobutyronitrile, propionitrile, and phenylacetonitrile, all of which have α-hydrogen atoms, instead of pivalonitrile in the 2nd reaction step, the yields of 4-cyanobiphenyl **2a** were 55%, 28%, and 0%, and biphenyl was obtained in 27%, 65%, and 99% yields, respectively (entries 9~11). Thus, nitriles bearing α-hydrogen atoms are not efficient in the present reaction, due to the α-proton abstraction of the nitriles by *n*-BuLi or by formed 4-biphenyl anion. On the other hand, when α,α-(dimethyl)phenylacetonitrile (2.0 equiv.) was used instead of pivalonitrile in the 2nd reaction step under the same procedure and conditions as those in entry 4, the yield of 4-cyanobiphenyl **2a** was slightly increased to 88% (entry 12).

Table 1. Optimization for Transformation of 4-Bromobiphenyl **1a** to 4-Cyanobiphenyl **2a**



	2nd step	3rd step	4th step	K_2CO_3	time	
entry	RCN	ROH	I_2 (equiv.)	(equiv.)	(h)	Yield (%)[a]
1	*t*-BuCN	H_2O[b]	1.5	3.0	1	35 (45)[c]
2	*t*-BuCN	MeOH	3.0	3.0	5	74 (13)[c]
3[d]	*t*-BuCN	MeOH	4.0	4.0	24	40 (38)[c]
4	*t*-BuCN	MeOH	4.0	4.0	6	84 (94)[e]
5[f]	*t*-BuCN	MeOH	4.0	4.0	6	81
6	*t*-BuCN	*t*-BuOH	4.0	4.0	6	70 (20)[c]
7	*t*-BuCN	CF_3CH_2OH	4.0	4.0	6	54 (33)[c]
8	*t*-BuCN	none	5.0	-	115	5 (68)[c] (10)[g]
9	*i*-PrCN	MeOH	4.0	4.0	6	55 (14)[c] (27)[h]
10	EtCN	MeOH	4.0	4.0	6	28 (65)[h]
11	$PhCH_2CN$	MeOH	4.0	4.0	6	0 (>99)[h]
12	$PhC(CH_3)_2CN$	MeOH	4.0	4.0	6	88
13[i]	*t*-BuCN	MeOH	4.0	4.0	6	0 (90)[c]
14[j]	*t*-BuCN	MeOH	4.0	4.0	6	0 (82)[c]

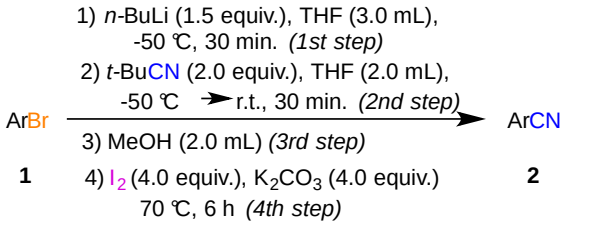
[a] Reaction was performed on a 3.0 mmol scale. Isolated yield.
[b] H_2O (4.0 mL) was used.
[c] Yield of *p*-biphenyl *t*-butyl ketone.
[d] 4th step reaction was carried out at 30 °C.
[e] Reaction was carried out with compound **1a** (6.0 mmol).
[f] 4th step reaction was carried out under irradiation with W-*hv* (300 W).
[g] Yield of compound **A'**
[h] Yield of biphenyl.
[i] BHT (2.0 equiv.) was added at 4th reaction step.
[j] TEMPO (2.0 equiv.) was added at 4th reaction step.



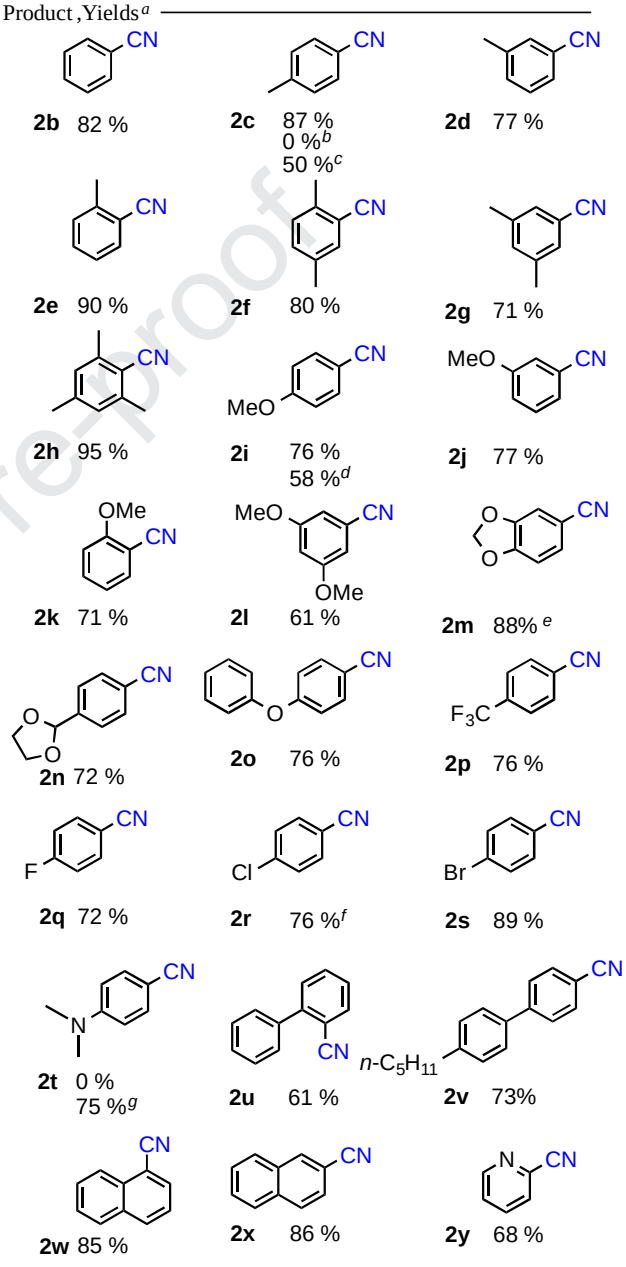
However, the complete separation and removal of excess α,α-(dimethyl)phenylacetonitrile from 4-cyanobiphenyl **2a** by chromatography on silica gel was very difficult. When the reactions in entry 4 were carried out in the presence of BHT (2,6-di-*t*-butyl-*p*-cresol, 2.0 equiv.) and TEMPO (2,2,6,6-tetramethylpiperidine 1-oxyl radical, 2.0 equiv.) in the 4th reaction step, 4-cyanobiphenyl **2a** was not obtained at all in both reactions. Instead, hydrolyzed *p*-biphenyl *t*-butyl ketone was obtained in 90% and 82% yields (entries 13, 14). Thus, those results and the formation of imine-coupling product **A'** (entry 8) suggest that the 4th reaction step is the radical-mediated reaction.

Based on those results, various aryl bromides **1** (3.0 mmol), such as phenyl bromide **1b**, *p*-methylphenyl bromide **1c**, *m*-methylphenyl bromide **1d**, *o*-methylphenyl bromide **1e**, 2,5-dimethylphenyl bromide **1f**, 3,5-dimethylphenyl bromide **1g**, and 2,4,6-trimethylphenyl bromide **1h**, in THF (3 mL) were treated with *n*-BuLi (1.5 equiv.) at -50 °C for 0.5 h to form the corresponding aryllithiums (1st step). Treatment of the aryllithiums with pivalonitrile (2.0 equiv.) in the temperature range of -50 °C to room temperature for 0.5 h (2nd step), followed by the reaction with MeOH (2.0 mL, 3rd step), and then with molecular iodine (4.0 equiv.) and K_2CO_3 (4.0 equiv.) at 70 °C for 6 h (4th step) gave the corresponding aromatic nitriles **2b**~**2h** in good yields, respectively, as shown in Scheme 1. Instead of *p*-methylphenyl bromide **1c**, treatment of *p*-methylphenyl chloride and *p*-methylphenyl iodide under the same procedure and conditions gave *p*-methylbenzonitrile **2c** in 0% and 50% yields, respectively. In the former case, *p*-methylphenyl chloride did not react with *n*-BuLi at all under the present reaction conditions. In the latter case, *p*-methylphenyl iodide reacted smoothly with *n*-BuLi to form *p*-methylphenyllithium and 1-iodobutane, which further reacted with formed *p*-methylphenyllithium in the 1st reaction step. The same successive treatment of aryl bromides **1** bearing an ether or a halogen group, such as *p*-methoxyphenyl bromide **1i**, *m*-methoxyphenyl bromide **1j**, *o*-methoxyphenyl bromide **1k**, 3,5-dimethoxyphenyl bromide **1l**, 4-bromo-1,2-methylenedioxybenzene **1m**, *p*-(1,3-dioxolan-2-yl)phenyl bromide **1n**, *p*-phenoxyphenyl bromide **1o**, *p*-(trifluoromethyl)phenyl bromide **1p**, *p*-fluorophenyl bromide **1q**, *p*-chlorophenyl bromide **1r**, and 1,4-dibromobenzene **1s** with *n*-BuLi (1st step), pivalonitrile (2nd step), MeOH (3rd step), and then with molecular iodine (4th step) gave also the corresponding aromatic nitriles **2i**~**2s** in good yields, respectively, as shown in Scheme 1. On the other hand, the same successive treatment of *p*-(*N*,*N*-dimethylamino)phenyl bromide **1t** did not generate *p*-(*N*,*N*-dimethylamino)benzonitrile **2t** at all. However, the same successive treatment of *p*-(*N*,*N*-dimethylamino)phenyl bromide **1t** with α,α-(dimethyl)phenylacetonitrile instead of pivalonitrile in the 2nd reaction step gave *p*-(*N*,*N*-dimethylamino)benzonitrile **2t** in 75% yield**.** When *o*-bromobiphenyl **1u**, 4-bromo-4'-pentylbiphenyl **1v**, 1-bromonaphthalene **1w**, 2-bromonaphthalene **1x**, and 2-bromopyridine **1y** were also treated with *n*-BuLi (1st step),

Scheme 1. Transformation of Aryl Bromides **1** into Aromatic Nitriles **2**



Product, Yields[a]

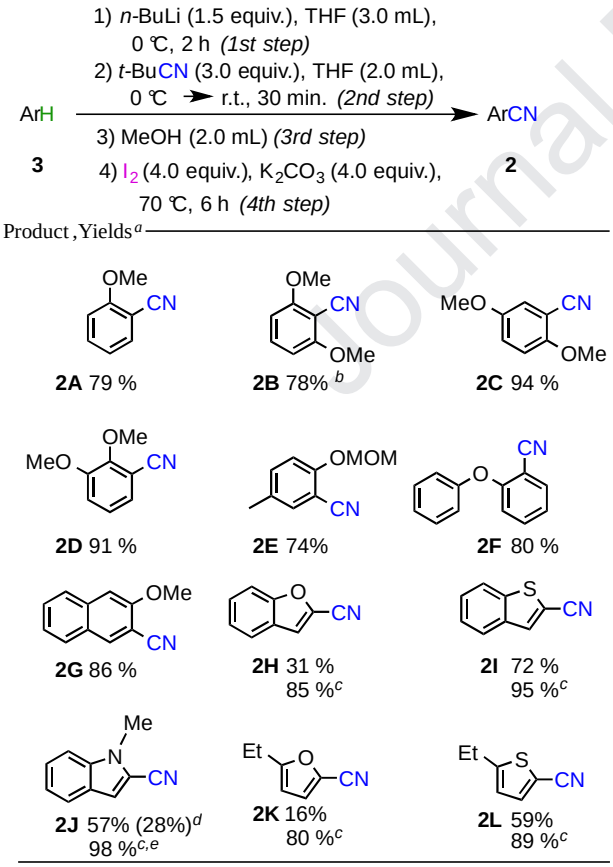


[a] Reaction was performed on 3.0 mmol scale. Isolated yield.
[b] *p*-Methylphenyl chloride was used as a starting material.
[c] *p*-Methylphenyl iodide was used as a starting material.
[d] *p*-Methoxyphenyl iodide was used as a starting material.
[e] *t*-BuCN (1.0 equiv.) was added and the 2nd step reaction was carried out for 7 min.
[f] I_2 (2.0 equiv.) was added and the 4th reaction step was carried out for 20 h.
[g] $PhC(CH_3)_2CN$ (2.0 equiv.) was used instead of *t*-BuCN.

pivalonitrile (2nd step), MeOH (3rd step), and then with molecular iodine (4th step) under the same procedure and conditions, the corresponding aromatic nitriles **2u**~**2y** were obtained in good yields, respectively, as shown in Scheme 1. Here, 4-cyano-4'-pentylbiphenyl **2v** is one of the typical liquid crystal materials, as shown in Fig. 1.

Then, to extend the synthetic utility of the present method, the present reaction was used for the transformation of arenes into aromatic nitriles. Thus, arenes **3** (3.0 mmol) bearing ether groups, such as anisole **3A**, 1,3-dimethoxybenzene **3B**, *p*-dimethoxybenzene **3C**, 1,2-dimethoxybenzene **3D**, *O*-MOM protected *p*-cresol **3E**, diphenyl ether **3F**, and 2-methoxynaphthalene **3G**, were treated with *n*-BuLi (1.5 equiv., 1st step) at 0 °C for 2 h, and then with pivalonitrile (3.0 equiv.) in the temperature range of 0 °C to room temperature for 0.5 h (2nd step). After the addition of MeOH (2.0 mL) to the reaction mixtures (3rd step), molecular iodine (4.0 equiv.) and K_2CO_3 (4.0 equiv.) were added, and the obtained mixtures were warmed at 70 °C for 6 h (4th step) to give the corresponding aromatic nitriles **2A**~**2G** in good yields, respectively, as shown in Scheme 2. In contrast, the same successive treatment of heteroaromatics, such as benzofuran **3H**, benzothiophene **3I**, *N*-methylindole **3J**, 2-ethylfuran **3K**, and 2-ethylthiophene **3L** gave the corresponding heteroaromatic nitriles **2H**~**2L** in moderate to low yields, respectively. However, when the successive reactions of heteroaromatics **3H**~**3L** with α,α-(dimethyl)phenylacetonitrile (2.0 equiv.) instead of pivalonitrile in the 2nd reaction step under the same procedure and conditions were carried out, the corresponding heteroaromatic nitriles **2H**~**2L** were obtained in good yields, as shown in Scheme 2. Here, the 4th reaction step with *N*-methylindole **3J** was carried out at 40 °C to suppress the iodination of the indole unit by molecular iodine.

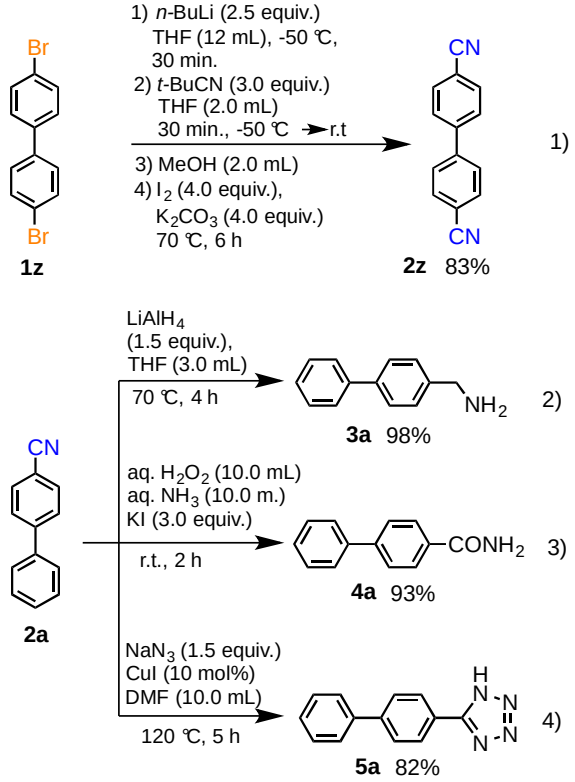
Scheme 2. Transformation of Arenes **3** into Aromatic Nitriles **2**



[a] Reaction was performed on 3.0 mmol scale. Isolated yield.
[b] 2nd step reaction was carried out for 3 h.
[c] $PhC(CH_3)_2CN$ (2.0 equiv.) was used instead of *t*-BuCN.
[d] Yield of 2-cyano-3-iodo-1-methylindole.
[e] 4th step reaction was carried out at 40 °C.

As a synthetic extension of the present method, 4,4'-dibromobiphenyl **1z** (3.0 mmol) in THF (12.0 mL) was treated with *n*-BuLi (2.5 equiv.) at -50 °C for 0.5 h to form the corresponding biaryldianion (1st step). Treatment of the biaryldianion with pivalonitrile (3.0 equiv.) in the temperature range of -50 °C to room temperature for 0.5 h (2nd step), followed by the reaction with MeOH (2.0 mL, 3rd step), and then with molecular iodine (4.0 equiv.) and K_2CO_3 (4.0 equiv.) at 70 °C for 6 h (4th step) gave 4,4'-dicyanobiphenyl **2z** in 83% yield, as shown in Scheme 3 (eq. 1). Once the aromatic nitriles are obtained, they can be smoothly transformed into the corresponding primary benzylic amines, aromatic amides, and 5-aryltetrazoles. For example, treatment of 4-cyanobiphenyl **2a** with $LiAlH_4$ in THF, with aq. NH_3 and aq. H_2O_2 in the presence of KI, and with NaN_3 in the presence of CuI in DMF gave 4-(aminomethyl)biphenyl **3a**, 4-biphenylcarboxamide **4a**, and 5-biphenyltetrazole **5a** in 98%, 93%, and 82% yields, respectively (eqs. 2~4).

Scheme 3. Synthetic Application.



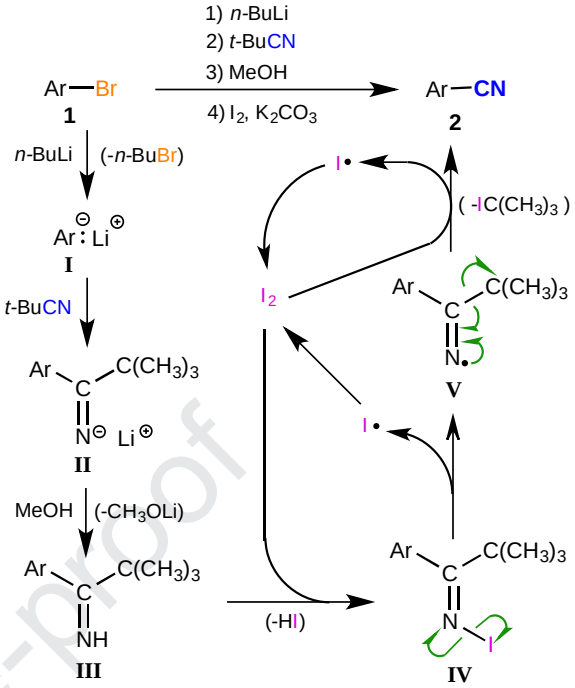
A possible reaction pathway for the present transformations of aryl bromides **1** into aromatic nitriles **2** is shown in Scheme 4. Aryllithium **I** formed from the reaction of aryl bromide **1** and *n*-BuLi, adds to pivalonitrile to form imino anion **II**, and the addition of MeOH generates imine **III**. Treatment of imine **III** with molecular iodine in the presence of K_2CO_3 generates *N*-iodo imine **IV**. Once *N*-iodo imine **IV** is formed, homolytic bond cleavage of the N-I bond occurs to form imino-nitrogen-centered radical, iminyl radical **V**. Finally, radical β-elimination of iminyl radical **V** occurs to generate aromatic nitrile **2** and a stable *t*-butyl radical, which further reacts with molecular iodine to form *t*-butyl iodide. When α,α-(dimethyl)phenylacetonitrile is used instead of pivalonitrile, radical β-elimination of the formed iminyl radical smoothly occurs to produce aromatic nitrile **2** and a rather stable α,α-dimethylbenzyl radical. Practically, when α,α-(dimethyl)phenylacetonitrile was used instead of pivalonitrile, α-methylstyrene and α,α-dimethylbenzyl methyl ether formed from the reaction of unstable α,α-dimethylbenzyl iodide and MeOH were observed. Moreover, when the present 4th reaction step was carried out in the presence of BHT (a hydrogen atom donor) and TEMPO (a radical trapping agent), the formation of aromatic nitrile **2** was completely inhibited, respectively. It is known that the homolytic bond cleavage of the N-I bond in *N*-iodosulfonamides under irradiation with a tungsten lamp occurs smoothly to form nitrogen-containing heterocyclic compounds with sulfonamides, (diacetoxyiodo)benzene (DIB), and iodine.[11]

Finally, aryl Grignard reagents (ArMgBr) instead of aryllithiums (ArLi) formed from aryl bromides and *n*-BuLi, could be used for the transformation of aryl bromides into aromatic nitriles in low to good yields depending on aryl bromides. However, in the 4th reaction step, the remained Mg (it is important to use excess Mg for effective formation of Grignard reagent) destroys I_2 soon, giving MgI_2. Thus, effective formation of *N*-iodoimines from the imines and I_2 is disturbed. This means that the yields of aromatic nitriles are going to be down as compared with those of aryllithiums with aryl bromides and *n*-BuLi (The present method). Additionally, reaction of ArMgBr with pivalonitrile requires long reaction time (12~24 h) at 70 °C in THF at 2nd reaction step. Consequently, the reaction with aryl Grignard reagents instead of aryllithiums is not effective and attractive to get aromatic nitriles.

3. Conclusion

Treatment of aryl bromides or arenes with *n*-BuLi, and then pivalonitrile, followed by the reaction with MeOH and then molecular iodine in the presence of K_2CO_3 under warming conditions gave the corresponding aromatic nitriles in good yields, respectively. By using the present methods, aromatic nitriles could be obtained effectively in one pot from aryl bromides and arenes under metal-cyanide-free and transition-metal-free conditions.

Scheme 4. Possible Reaction Pathway for Aromatic Nitriles **2**.



4. Experimental Section

4.1 General: ^{1}H NMR spectra were measured on a JEOL ECS-400 (400 MHz) spectrometer. Chemical shifts were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; sext = sextet; m = multiplet), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on a JEOL ECS-400 (100 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm). High-resolution mass spectra (HRMS) were recorded by Thermo Fisher Scientific Exactive Orbitrap mass spectrometer. Characteristic peaks in the infrared (IR) spectra were recorded on a JASCO FT/IR-4100 spectrometer. Melting points were determined using a Yamato Melting Point Apparatus Model MP-21. Thin-layer chromatography (TLC) was performed using 0.25 mm silica gel plates (60F254). The products were purified by column chromatography on neutral silica gel 60 (63–200 mesh).

4.2 Typical Procedure (1): Transformation of 4-Bromobiphenyl 1a into 4-Cyanobiphenyl 2a: To a solution of 4-bromobiphenyl **1a** (3.0 mmol, 699.3 mg) in THF (3.0 mL) was added *n*-BuLi (4.5 mmol, 1.55 M in hexane, 2.87 mL) at -50 °C.

The obtained mixture was stirred for 30 min at -50 °C under an argon atmosphere. Pivalonitrile (6.0 mmol, 498.8 mg) in THF (2.0 mL) was added to the mixture at -50 °C and the obtained mixture was stirred for 30 min in the temperature range of -50 °C to room temperature. MeOH (2.0 mL) was added to the mixture. Then, I_2 (12.0 mmol, 3045.6 mg) and K_2CO_3 (12.0 mmol, 1658.4 mg) were added to the mixture at room temperature, and the obtained mixture was stirred for 6 h at 70 °C. Sat. aq. Na_2SO_3 solution (20.0 mL) was added to the reaction mixture, and the product was extracted with AcOEt (10.0 mL × 3). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (chloroform: *n*-hexane = 1:1) to give 4-cyanobiphenyl **2a** (451.6 mg, 84%).

4.2.1 4-Cyanobiphenyl (2a): Yield: 451.6 mg (84%); white solid (commercially available); Mp: 84 °C; IR (neat) 2225 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.41 (t, 1H, *J* = 7.3 Hz), 7.47 (t, 2H, *J* = 7.3 Hz), 7.58 (d, 2H, *J* = 7.3 Hz), 7.68 (d, 2H, *J* = 8.8 Hz), 7.73 (d, 2H, *J* = 8.8 Hz); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 110.8, 118.9, 127.2, 127.7, 128.6, 129.1, 132.5, 139.1, 145.6.

4.2.2 Benzonitrile (2b): Yield: 253.7 mg (82%); colorless liquid (commercially available); IR (neat) 2228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.48 (t, 2H, *J* = 7.7 Hz), 7.61(tt, 1H, *J* = 7.7, 1.4 Hz), 7.66 (dd, 1H, *J* = 7.7, 1.4 Hz); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 112.3, 118.8, 129.0, 132.0, 132.7.

4.2.3 4-Methylbenzonitrile (2c): Yield: 305.8 mg (87%); yellow liquid (commercially available); IR (neat) 2228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3H), 7.26 (d, 2H, *J* = 7.2 Hz), 7.51 (d, 2H, *J* = 7.2 Hz); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 21.5, 108.9, 118.9, 129.6, 131.7, 143.5.

4.2.4 3-Methylbenzonitrile (2d): Yield: 270.6 mg (77%); colorless liquid (commercially available); IR (neat) 2228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3H), 7.33-7.37 (m, 1H), 7.40-7.42 (m, 1H), 7.45-7.47 (m, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 21.1, 112.1, 119.0, 128.9, 129.2, 132.4, 133.6, 139.1.

4.2.5 2-Methylbenzonitrilez (2e): Yield: 316.3 mg (90%); Oil (commercially available); IR (neat) 2225 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3H), 7.26 (t, 1H, *J* = 7.6 Hz), 7.31 (d, 1H, *J* = 7.6 Hz), 7.48 (dd, 1H, *J* = 7.7, 7.6 Hz), 7.58 (d, 1H, *J* = 7.7 Hz); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 20.5, 112.7, 118.1, 126.2, 130.2, 132.5, 132.6, 141.9.

4.2.6 2,5-Dimethylbenzonitrile (2f): Yield: 314.8mg (80%); Oil; IR (neat) 2227 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3H), 2.50 (s, 3H), 7.19 (d, 1H, *J* = 8.1 Hz), 7.27 (d, 1H, *J* = 8.1 Hz), 7.40 (s, 1H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 19.9, 20.6, 112.5, 118.3, 130.1, 132.7, 133.5, 136.0, 138.8; HRMS (ESI) Calcd for $C_9H_{10}N$ $[M+H]^+$ = 132.0808, Found = 132.0812 .

4.2.7 3,5-Dimethylbenzonitrile (2g): Yield: 275.5 mg (70%); white solid; Mp: 42-43 °C; IR (neat) 2229 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 6H), 7.22 (s, 1H), 7.26 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 21.0, 112.0, 119.2, 129.7, 134.6, 139.0, HRMS (ESI) Calcd for $C_9H_{10}N$ $[M+H]^+$ = 132.0808, Found = 132.0811.

4.2.8 2,4,6-Trimethylbenzonitrile (2h): Yield: 413.9 mg (95%); yellow solid (commercially available); Mp: 42-43 °C; IR (neat) 2216 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 3H), 2.48 (s, 6H), 6.93 (s, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 20.6, 21.5, 110.2, 117.6, 128.1, 141.9, 142.7.

4.2.9 4-Methoxybenzonitrile (2i): Yield: 303.6 mg (76%); white solid (commercially available); Mp: 60-61 °C; IR (neat) 2217 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.87 (s, 3H), 6.96 (d, 2H, *J* = 9.0 Hz), 7.60 (d, 2H, *J* = 9.0 Hz); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 55.4, 103.7, 114.6, 119.1, 133.8, 162.7.

4.2.10 3-Methoxybenzonitrile (2j): Yield: 307.6 mg (77%); oil (commercially available); IR (neat) 2230 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3H), 7.13-7.15 (m, 2H),

7.24-7.26 (m, 1H), 7.36-7.40 (m, 1H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 55.5, 113.1, 116.8, 118.7, 119.3, 124.5, 130.3, 159.6.

4.2.11 2-Methoxybenzonitrile (2k): Yield: 283.6 mg (71%); Oil (commercially available); IR (neat) 2228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.94 (s, 3H), 6.97-7.03 (m, 2H), 7.50-7.58 (m, 2H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 55.9, 101.7, 111.2, 116.5, 120.7, 133.7, 134.4, 161.2.

4.2.12 3,5-Dimethoxybenzonitrile (2l): Yield: 298.6 mg (61%); white solid (commercially available); Mp: 86-87 °C; IR (neat) 2229 cm^{-1} ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 6H), 6.66 (t, 1H, *J* = 2.4 Hz), 6.77 (d, 2H, *J* = 2.4 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 55.6, 105.6, 109.8, 113.3, 118.7, 160.9.

4.2.13 1,3-Benzodioxole-5-carbonitrile (2m): Yield: 388.4 mg (88%); white solid (commercially available); Mp: 89-90 °C; IR (neat) 2221 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 6.07 (s, 2H), 6.87 (d, 1H, *J* = 8.1 Hz), 7.04 (d, 1H, *J* = 1.6 Hz), 7.21 (dd, 1H, *J* = 8.1, 1.6 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 102.2, 104.9, 109.1, 111.4, 118.8, 128.2, 148.0, 151.5.

4.2.14 4-(1,3-Dioxolan-2-yl)benzonitrile (2n): Yield: 378.4 mg (72%); white solid; Mp: 33-34 °C; IR (neat) 2228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.04-4.08 (m, 2H), 4.09-4.13 (m, 2H), 5.81 (s, 1H), 7.60 (d, 2H, *J* = 8.3 Hz), 7.68 (d, 2H, *J* = 8.3 Hz) ; $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 65.4, 102.4, 112.9, 118.6, 127.2, 132.2, 143.0; HRMS (ESI) Calcd for $C_{10}H_{10}NO_2$ $[M+H]^+$ = 176.0707, Found = 176.0706.

4.2.15 4-Phenoxybenzonitrile (2o): Yield: 445.1 mg (76%) (commercially available); yellow liquid; IR (neat) 2226 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.01 (d, 2H, *J* = 9.1 Hz), 7.07 (dd, 2H, *J* = 8.5, 1.1 Hz), 7.24 (tt, 1H, *J* = 7.5, 1.1 Hz), 7.42 (dd, 2H *J* = 8.5, 7.5 Hz), 7.60 (d, 2H, *J* = 9.1 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 105.7, 117.8, 118.8, 120.4, 125.1, 130.2, 134.1, 154.7, 161.6.

4.2.16 4-(Trifluoromethyl)benzonitrile (2p): Yield: 390.2 mg (76%); white solid (commercially available); Mp: 36 °C; IR (neat) 2236 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, 2H, *J* = 8.2 Hz), 7.82 (d, 2H, *J* = 8.2 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 116.0, 117.4, 123.0 (q, *J* = 272.8 Hz), 126.1 (q, *J* = 3.8 Hz), 132.6, 134.4 (q, *J* = 33.3 Hz).

4.2.17 4-Fluorobenzonitrile (2q): Yield: 261.6 mg (72%); white solid (commercially available); Mp: 35-36 °C; IR (neat) 2233 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.16-7.21 (m, 2H), 7.66-7.71 (m, 2H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 108.6, 116.9 (d, *J* = 22.6 Hz), 118.0, 134.7 (d, *J* = 9.4 Hz), 165.0 (d, *J* = 256.5 Hz).

4.2.18 4-Chlorobenzonitrile (2r): Yield: 313.7 mg (76%); white solid (commercially available); Mp: 90-91 °C; IR (neat) 2225 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, 2H, *J* = 8.6 Hz), 7.59 (d, 2H, *J* = 8.6 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 110.7, 118.0, 129.7, 133.3, 139.5.

4.2.19 4-Bromobenzonitrile (2s): Yield: 486.0 mg (89%); white solid (commercially available); Mp: 107-108 °C; IR (neat) 2224 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, 2H, *J* = 8.8 Hz), 7.64 (d, 2H, *J* = 8.8 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 111.2, 118.0, 128.0, 132.6, 133.4.

4.2.20 4-(Dimethylamino)benzonitrile (2t): Yield: 328.9 mg (75%); brown solid (commercially available); Mp: 69-70 °C; IR (neat) 2212 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.04 (s, 6H), 6.64 (d, 2H, *J* = 9.1 Hz), 7.47 (d, 2H, *J* = 9.1 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 39.9, 97.2, 111.3, 120.7, 133.3, 152.4.

4.2.21 2-Cyanobiphenyl (2u): Yield: 328.0 mg (61%); yellow liquid; IR (neat) 2224 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.42-7.57 (m, 7H), 7.65 (t, 1H, *J* = 7.6 Hz), 7.77 (d, 1H, *J* = 7.6 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 111.2, 118.7, 127.5 (2C), 128.67, 128.69, 130.0, 132.8, 133.7, 138.1, 145.4; HRMS (ESI) Calcd for $C_{13}H_{10}N$ $[M+H]^+$ = 189.0808 Found = 180.0813.

4.2.22 4-Cyano-4'-pentylbiphenyl (2v): Yield: 546.1 mg (73%); yellow liquid (commercially available); IR (neat) 2225 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.0 Hz), 1.32-1.38 (m, 4H), 1.65 (quin, 2H, *J* = 7.5 Hz), 2.66 (t, 2H, *J* = 7.5 Hz), 7.29 (d, 2H, *J* = 8.2 Hz), 7.51 (d, 2H, *J* = 8.2 Hz), 7.67 (d, 2H, *J* = 8.6 Hz), 7.71 (d, 2H, *J* = 8.6 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 14.0, 22.5, 31.1, 31.5, 35.6, 110.5, 119.1, 127.0, 127.5, 129.2, 132.5, 136.4, 143.8, 145.6.

4.2.23 1-Naphthonitrile (2w): Yield: 390.6 mg (85%); yellow liquid (commercially available); IR (neat) 2221 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.51 (dd, 1H, *J* = 8.2, 2.2 Hz), 7.61 (td, 1H, *J* = 7.6, 7.0 Hz), 7.69 (td, 1H, *J* = 8.3, 7.0 Hz), 7.89-7.93 (m, 2H), 8.07 (d, 1H, *J* = 8.3 Hz), 8.23 (d, 1H, *J* = 8.3 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 110.1, 117.8, 124.9, 125.1, 127.5, 128.5, 128.6, 132.3, 132.6, 132.8, 133.2,.

4.2.24 2-Naphthonitrile (2x): Yield: 395.2 mg (86%); white solid (commercially available); Mp: 62-63 °C; IR (neat) 2227 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.57-7.68 (m, 3H), 7.66-7.94 (m, 3H), 8.24 (s, 1H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 109.4, 119.3, 126.3, 127.6, 128.0, 128.4, 129.0, 129.2, 132.2, 134.2, 134.6.

4.2.25 2-Cyanopyridine (2y): Yield: 212.4 mg (68%); yellow liquid (commercially available); IR (neat) 2236 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.54 (td, 1H, *J* = 4.7, 1.5 Hz), 7.72 (d, 1H, *J* = 7.7 Hz), 7.86 (td, 1H, *J* = 7.7, 1.5 Hz), 8.74 (d, 1H, *J* = 4.7 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 117.1, 126.9, 128.5, 134.0, 137.0, 151.1.

4.2.26 4,4'-Dicyanobiphenyl (2z): Yield: 508.5 mg (83%); white solid (commercially available); Mp: 226-227 °C; IR (neat) 2226 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, 4H, *J* = 8.6 Hz), 7.79 (d, 4H, *J* = 8.6 Hz); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$): δ = 112.4, 118.4, 127.9, 132.9, 143.5.

4.3 Typical Procedure (2): Transformation of Anisole 3A into 2-Methoxybenzonitrile 2A: To a solution of anisole **3A** (3.0 mmol, 324.4 mg) in THF (3.0 mL) was added *n*-BuLi (4.5 mmol, 1.55 M in hexane, 2.87 mL) at 0 °C. The mixture was stirred for 2 h at 0 °C under an argon atmosphere. Then, pivalonitrile (9.0 mmol, 748.2 mg) in THF (2.0 mL) was added to the mixture at 0 °C and the obtained mixture was stirred for 30 min in the temperature range of 0 °C to room temperature. MeOH (2.0 mL) was added to the mixture. Then, I_2 (12.0 mmol, 3045.6 mg) and K_2CO_3 (12.0 mmol, 1658.4 mg) were added to the mixture at room temperature, and the obtained mixture was stirred for 6 h at 70 °C. Sat. aq. Na_2SO_3 solution (20.0 mL) was added to the

reaction mixture, and the product was extracted with AcOEt (10.0 mL × 3). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (chloroform: *n*-hexane = 1:1) to give 2-methoxybenzonitrile **2A** (315.6 mg, 79%).

4.3.1 2-Methoxybenzonitrile (2A): Yield: 315.6 mg (79%); Oil (commercially available); IR (neat) 2228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.94 (s, 3H), 6.97-7.03 (m, 2H), 7.50-7.58 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 55.9, 101.7, 111.2, 116.5, 120.7, 133.7, 134.4, 161.2.

4.3.2 2,6-Dimethoxybenzonitrile (2B): Yield: 381.8 mg (78%); yellow solid (commercially available); Mp: 113-114 °C; IR (neat) 2229 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 6 H), 6.55 (d, 2H, *J* = 8.5 Hz), 7.44 (t, 1H, *J* = 8.5 Hz); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 56.2, 91.3, 103.8, 104.4, 134.6, 162.7.

4.3.3 2,5-Dimethoxybenzonitrile (2C): Yield: 460.2 mg (94%); yellow solid (commercially available); Mp: 79-80 °C; IR (neat) 2224 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 3 H), 3.89 (s, 3H), 6.90 (d, 1H, *J* = 9.1 Hz), 7.06 (d, 1H, *J* = 3.2 Hz), 7.10 (dd, 1H, *J* = 9.1, 3.2 Hz); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 55.9, 56.4, 101.7, 112.5, 116.4, 117.5, 120.8, 153.1, 155.7.

4.3.4 2,3-Dimethoxybenzonitrile (2D): Yield: 445.5 mg (91%); yellow solid (commercially available); Mp: 47 °C; IR (neat) 2230 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.90 (s, 3H), 4.03 (s, 3H), 7.10-7.16 (m, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 56.0, 61.6, 106.9, 116.2, 116.9, 124.4 (2C), 151.6, 152.6.

4.3.5 2-(Methoxymethoxy)-5-methylbenzonitrile (2E): Yield: 393.4 mg (74%); yellow liquid; IR (neat) 2226 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 3.52 (s, 3H), 5.26 (s, 2H), 7.12 (d, 1H, *J* = 8.6 Hz), 7.31 (dd, 1H, *J* = 8.6, 1.6 Hz), 7.37 (d, 1H, *J* = 1.6 Hz); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 20.2, 56.5, 94.8, 102.5, 114.9, 116.5, 131.6, 133.5, 135.0, 157.0; HRMS (ESI) Calcd for $C_{10}H_{12}NO_2$ $[M+H]^+$ = 178.0863, Found = 178.0859.

4.3.6 2-Phenoxybenzonitrile (2F): Yield: 468.5 mg (80%); yellow liquid; IR (neat) 2230 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 6.86 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.09 (dd, 2H, *J* = 7.6, 1.1 Hz), 7.13 (td, 1H, *J* = 8.5, 7.6 Hz), 7.22 (tt, 1H, *J* = 7.6, 1.1 Hz), 7.41 (t, 2H, *J* = 7.6 Hz), 7.47 (td, 1H, *J* = 8.5, 7.7 Hz), 7.66 (dd, 1H, *J* = 7.7, 1.6 Hz); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 103.6, 116.0 116.9, 120.0, 122.7, 125.0, 130.1, 133.8, 134.2, 154.9, 159.7; HRMS (ESI) Calcd for $C_{13}H_{10}NO$ $[M+H]^+$ = 196.0757 Found = 196.0753.

4.3.7 3-Methoxy-2-naphthonitrile (2G): Yield: 472.7 mg (86%); white solid; Mp: 123-124 °C; IR (neat) 2224 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.03 (s, 3H), 7.19 (s, 1H), 7,43 (dd, 1H, *J* = 8.3, 7.5 Hz), 7.58 (dd, 1H, *J* = 8.3, 7.5 Hz), 7.76 (d, 1H, *J* = 8.3 Hz) 7.80 (d, 1H, *J* = 8.3 Hz), 8.15 (s, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 56.0, 103.4, 106.2, 116.5, 125.1, 126.8, 127.4, 128.2, 129.4, 136.0, 136.2, 156.2; HRMS (ESI) Calcd for $C_{12}H_{10}ON$ $[M+H]^+$ = 184.0757, Found = 184.0760.

4.3.8 2-Benzofurancarbonitrile (2H): Yield: 365.02 mg (85%); yellow solid; Mp: 34-35°C; IR (neat) 2234 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.37 (td, 1H, *J* = 8.0, 7.0 Hz), 7.47 (s, 1H), 7.52 (td, 1H, *J* = 8.5, 7.0 Hz), 6.57 (d, 1H, *J* = 8.5 Hz), 7.69 (d, 1H, *J* = 8.0 Hz); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 111.8, 112.1, 118.5, 122.6, 124.5, 125.5, 127.3, 128.4, 155.7; HRMS (ESI) Calcd for C_9H_6NO $[M+H]^+$ = 144.0444, Found = 144.0444.

4.3.9 2-Benzothiophenecarbonitrile (2I): Yield: 453.7 mg (95%); yellow liquid; IR (neat) 2216 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.48 (td, 1H, *J* = 8.0, 7.0 Hz), 7.54 (td, 1H, *J* = 8.0, 7.7 Hz), 7.86-7.91 (m, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 109.6, 114.5, 122.3, 125.2, 125.7, 127.8, 135.0, 137.4, 141.2; HRMS (ESI) Calcd for C_9H_6NS $[M+H]^+$ = 160.0125, Found = 160.0125.

4.3.10 2-Cyano-1-methylindole (2J): Yield: 459.2 mg (98%); yellow solid; Mp: 70 °C; IR (neat) 2221 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 3H), 7.16 (s, 1H), 7.21 (dd, 1H, *J* = 8.0, 6.8 Hz), 7.36 (d, 1H, *J* = 8.0 Hz), 7.41 (dd, 1H, *J* = 8.3, 6.8 Hz), 7.67 (d, 1H, *J* = 8.3 Hz); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 31.5, 110.06, 110.14, 112.6, 113.6, 121.3, 122.3, 125.8, 126.0, 137.9; HRMS (ESI) Calcd for $C_{10}H_9N_2$ $[M+H]^+$ = 157.0760, Found = 157.0765.

4.3.11 2-Cyano-5-ethylfuran (2K): Yield: 290.7 mg (80%); yellow liquid; IR (neat) 2228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, 3H, *J* = 7.6 Hz), 2.71 (q, 2H, *J* = 7.6 Hz), 6.13 (d, 1H, *J* = 3.5 Hz), 7.01 (d, 1H, *J* = 3.5 Hz); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 11.6, 21.6, 106.2, 112.0, 123.1, 124.2, 163.6; HRMS (ESI) Calcd for C_7H_8NO $[M+H]^+$ = 122.0600, Found = 122.0600.

4.3.12 2-Cyano-5-ethylthiophene (2L): Yield: 366.3 mg (89%); yellow liquid; IR (neat) 2217 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.34 (t, 3H, *J* = 7.5 Hz), 2.90 (q, 2H, *J* = 7.5 Hz), 6.81 (d, 1H, *J* = 3.6 Hz), 7.46 (d, 1H, *J* = 3.6 Hz), $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 15.6, 23.6, 106.7, 114.7, 124.3, 137.7, 155.8; HRMS (ESI) Calcd for C_7H_8NS $[M+H]^+$ = 138.0372, Found = 138.0376.

4.4 Procedure for Transformation of 4-Cyanobiphenyl 2a into 4-(Aminomethyl)biphenyl 3a: To a solution of 4-cyanobiphenyl **2a** (1.0 mmol, 179.2 mg) in THF (8.0 mL) were slowly added $LiAlH_4$ (1.5 mmol, 56.9 mg) at 0 °C. The obtained mixture was stirred for 4 h at 70 °C. Water (5 mL) and aq. NaOH 1 M, 10.0 mL) were added to the reaction mixture. The aqueous layer was extracted with $CHCl_3$ (5.0 mL × 3). The organic layer was washed with brine, dried over Na_2SO_4, and filtered through celite. The solvent was removed under reduced pressure to give 4-(aminomethyl)biphenyl **3a** (179.6 mg, 98%).

4.4.1 4-(Aminomethyl)biphenyl (3a): Yield: 179.6 mg (98%); white solid; Mp 128-129 °C: IR (neat) 3269 (br), 2630, 1586, 1485, 1396, 1304, 1245, 1131, 986 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.93 (s, 2H), 7.34 (t, 1H, *J* = 7.4 Hz), 7.39 (d, 2H, *J* = 8.2 Hz), 7.44 (dd, 2H, *J* = 7.7, 7.4 Hz), 7.57-7.61 (m, 4H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ = 46.2, 127.0, 127.2, 127.3, 127.5, 128.7, 139.8, 140.9, 142.4; HRMS (ESI) Calcd for $C_{13}H_{14}N$ $[M+H]^+$ = 184.1121, Found = 184.1120.

4.5 Procedure for Transformation of 4-Cyanobiphenyl 2a into 4-Biphenylcarboxamide 4a: To a solution of 4-cyanobiphenyl **2a** (1.0 mmol, 179.2 mg) in THF (8.0 mL) were added aq. NH_3 (28%, 10.0 mL) and KI (3.0 mmol, 498.0 mg) at 0 °C. Aq. H_2O_2 (30%, 10.0 mL) was added dropwise to the mixture. The obtained

mixture was stirred for 2 h at room temperature. Sat. aq. Na_2SO_3 solution (20.0 mL) was added to the reaction mixture and the product was extracted with AcOEt (10.0 mL × 3). The organic layer was dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure to give 4-biphenylcarboxamide **4a** (183.4 mg, 93%).

4.5.1 4-Biphenylcarboxamide (4a): Yield: 183.4 mg (93%); white solid; Mp 223 °C: IR (neat) 3404, 3170, 1644, 1614, 1407 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 6.51-5.54 (m, 2H), 6.61 (dd, 2H, *J* = 6.8, 7.7 Hz), 6.84-6.89 (m, 4H), 7.10 (d, 2H, *J* = 6.8 Hz), 7.17 (s, 1H); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ = 126.5, 126.9, 128.0, 128.2, 129.0, 133.1, 139.2, 142.8, 167.6; HRMS (ESI) Calcd for $C_{13}H_{12}ON$ $[M+H]^+$ = 198.0913, Found = 198.0915.

4.6 Procedure for Transformation of 4-Cyanobiphenyl 2a into 5-(Bipheny-4'-yl)-1*H*-tetrazolel 5a: To a solution of 4-cyanobiphenyl **2a** (1.0 mmol, 179.2 mg) in DMF (10.0 mL) were added CuI (0.25 mmol, 47.6 mg) and NaN_3 (1.5 mmol, 97.5 mg). The obtained mixture was stirred for 5 h at 120 °C. The mixture was cooled to room temperature and then, sat. aq. $NaHCO_3$ (15.0 mL) and water (5.0 mL) were added. The aqueous layer was washed with AcOEt (5.0 mL × 3), and then acidified with aq. 1.0 HCl (1 M) to become pH 2. The aqueous layer was extracted with AcOEt (5.0 mL × 3). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent, the residue was purified by neutral silica-gel column chromatography (eluent: AcOEt) to give 5-(bipheny-4'-yl)-1*H*-tetrazolel **5a** (182.2 mg, 82%).

4.6.1 5-(Bipheny-4'-yl)-1*H*-tetrazole (5a): Yield: 182.2 mg (82%); white solid; Mp 248–249 °C, (lit.[12] Mp 247-249 °C): IR (neat) 2727, 1614, 1426, 1159, 1055, 991, 849, 744, 695 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 7.41 (t, 1H, *J* = 7.3 Hz), 7.50 (dd, 2H, *J* = 7.5, 7.3 Hz), 7.75 (d, 2H, *J* = 7.5 Hz), 7.91 (d, 2H, *J* = 7.8 Hz), 8.13 (d, 2H, *J* = 7.8 Hz); ^{13}C{^{1}H}NMR (100 MHz, DMSO-d_6): δ = 123.2, 126.8, 127.6 (2C), 128.2 (2C), 129.1, 138.9, 142.7; HRMS (ESI) Calcd for $C_{13}H_{11}N_4$ $[M+H]^+$ = 223.0978, Found = 223. 0974.

4.7.1 Dimer A': white solid; Mp: 166-167 °C; IR (neat) 1600, 1487, 1202, 987, 836, 769 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.95 (s, 18H), 7.11 (d, 4H, *J* = 7.6 Hz), 7.37 (t, 2H, *J* = 7.1 Hz), 7.47 (d, 4H, *J* = 7.6 Hz), 7.61 (d, 4H, *J* = 7.6 Hz), 7.65 (d, 4H, *J* = 7.6 Hz); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 28.3, 38.1, 126.1, 127.0, 127.4, 127.9, 128.8, 135.9, 139.9, 140.7, 165.5; HRMS (ESI) Calcd for $C_{34}H_{37}N_2$ $[M+H]^+$ = 473.2951, Found = 472.2951

□□□□□ **α,α-(Dimethyl)phenylacetonitrile:** yellow liquid; Bp: 63 °C/ 1 mmHg; IR (neat) 2236 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.74 (s, 6H), 7.32 (t, 1H, *J* = 8.0 Hz), 7.40 (t, 2H, *J* = 8.0 Hz), 7.48 (d, 2H, *J* = 8.0 Hz); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 29.1, 37.1, 124.5, 125.0, 127.7, 128.8, 141.3; HRMS (ESI) Calcd for $C_{10}H_{12}N$ $[M+H]^+$ = 146.0964, Found = 146.0964.

4.7.3 2-Cyano-3-iodo-1-methylindole: Yield: 237.6 mg (28%); yellow solid; Mp: 94-95 °C; IR (neat) 2221 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.96 (s, 3H), 7.27-7.25 (m, 2H), 7.44-7.49 (m, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ = 32.4, 69.2, 110.3, 113.2, 115.5, 122.2, 122.8, 126.8, 129.2, 137.7; HRMS (ESI) Calcd for $C_{10}H_8N_2I$ $[M+H]^+$ = 281.9648, Found = 281.9650 .

Supporting Information (see footnote on the first page of this article): … . Copies of the ^{1}H NMR and ^{13}C NMR spectra of all aromatic nitriles **2a**~**2z**, **2A**~**2L**, dimer **A'**, and derivatives **3a**~**5a**.

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